JPRS-USB-85-003

18 April 1985

USSR Report

SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 19, No. 1, January-February 1985

FBIS FOREIGN BROADCAST INFORMATION SERVICE

NOTE

JPRS publications contain information primarily from foreign newspapers, periodicals and books, but also from news agency transmissions and broadcasts. Materials from foreign-language sources are translated; those from English-language sources are transcribed or reprinted, with the original phrasing and other characteristics retained.

Headlines, editorial reports, and material enclosed in brackets [] are supplied by JPRS. Processing indicators such as [Text] or [Excerpt] in the first line of each item, or following the last line of a brief, indicate how the original information was processed. Where no processing indicator is given, the information was summarized or extracted.

Unfamiliar names rendered phonetically or transliterated are enclosed in parentheses. Words or names preceded by a question mark and enclosed in parentheses were not clear in the original but have been supplied as appropriate in context. Other unattributed parenthetical notes within the body of an item originate with the source. Times within items are as given by source.

The contents of this publication in no way represent the policies, views or attitudes of the U.S. Government.

PROCUREMENT OF PUBLICATIONS

JPRS publications may be ordered from the National Technical Information Service (NTIS), Springfield, Virginia 22161. In ordering, it is recommended that the JPRS number, title, date and author, if applicable, of publication be cited.

Current JPRS publications are announced in Government Reports Announcements issued semimonthly by the NTIS, and are listed in the Monthly Catalog of U.S. Government Publications issued by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Correspondence pertaining to matters other than procurement may be addressed to Joint Publications Research Service, 1000 North Glebe Road, Arlington, Virginia 22201.

JPRS-USB-85-003

18 April 1985

USSR REPORT

SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 19, No. 1, January-February 1985

Translation of the Russian-language bimonthly journal KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA published in Moscow by Izdatel'stvo "Meditsina"

CONTENTS

Factor Analysis of Reaction to Lower Body Negative Pressure Test on the Ground and During Spaceflight 1

Effect of Spaceflight Factors on Hormonal Regulation of Fluid-Electrolyte Metabolism 4

Effect of Space Diet on Blood Valine Content 9

Operator's Mental Adaptation and Work Capacity in Simulated Weightlessness 22

Effect of Rotation and Vibration on Human Orientation Relative to Gravity Vertical 30

Rheological Parameters of Blood at Different Levels of Motor Activity 37

Comparative Characteristics of Central Hemodynamics and Circulatory Redistribution Reactions to Active and Passive Orthostatic Tests .. 42

Amino Acid Composition of Human Blood Serum During Immersion Hypokinesia 53

Effect of Long-Term Hypokinesia on Blood Serum Lipid Spectrum 57

Distinctive Changes in Regional Hemodynamics and Gas Exchange in Healthy Man in Response to Moderate Phlebotomy and Reinfusion of Blood After Submitting to Antiorthostatic Hypokinesia 63

Activation of Lipid Peroxidation in the Liver Under Hypokinetic Conditions and Its Prevention With Antioxidants 68

Specificity of Ultrastructural Changes in Rat Myocardium Submitted to Hypokinesia and Radiation Damage 75

Lenticular Opacities in Mice Exposed to Helium Ions With Energy of 4 GeV/Nucleon and ^{60}Co Gamma Radiation 80

Skin Lesions After Exposure to High-Energy Protons and Helium Ions ... 84

Effect of Flight Aboard Cosmos-1129 Biosatellite on Thyroid Hormone Levels in Rat Blood and Thyroid Tissue 89

Prospects of Using Unicellular Algae Protein in Biological Life-Support Systems 94

Investigation of Toxic Properties of Preservatives to be Used in Water Recycling Systems 100

Relevance of Water Structure to Assessment of Quality of Recycled of Quality of Recycled Water 105

Mathematical Model of Cyclic Kinetics of Granulocytopoiesis 111

Methods for Measuring External Respiration and Gas Exchange Parameters of Macaca Rhesus Monkeys 117

Investigation of Growth Rate of Methane-Assimilating Bacteria in Weightlessness 121

Prediction of Classes M and X X-Ray Phenomena 125

New Book of Selected Lectures on Aviation Medicine 129

Synopses of Articles Filed With the All-Union Scientific Research Institute of Medical and Medicotechnical Information and All-Union Institute of Scientific and Technical Information 131

Index of Articles: KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, Volume 18, Numbers 1-6, 1984 137

Author Index: KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, Volume 18, Numbers 1-6, 1984 147

PUBLICATION DATA

English title	:	SPACE BIOLOGY AND AEROSPACE MEDICINE
Russian title	:	KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA
Editor	:	O. G. Gazenko
Publishing house	:	Meditsina
Place of publication	:	Moscow
Date of publication	:	January-February 1985
Signed to press	:	7 December 1984
Copies	:	1450
COPYRIGHT	:	"Kosmicheskaya biologiya i aviakosmicheskaya meditsina", 1985

EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 629.78:612.014.477-064

FACTOR ANALYSIS OF REACTION TO LOWER BODY NEGATIVE PRESSURE TEST ON THE GROUND AND DURING SPACEFLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 20 Oct 83) pp 4-5

[Article by A. D. Voskresenskiy, V. A. Degtyarev, V. G. Doroshev and S. L. Chekanova]

[English abstract from source] The method of main components was used to examine separately the cosmonauts' responses to LBNP tests on the ground and in space flight. The factor structures of the ground and flight data did not show significant differences. In both cases the first factor can be termed the factor of venous return and the second, the factor of the cardiac state. The first two factors were responsible for about 60%, and the first three factors for 76-78% of data scatter. The observation that the factor structure remains unchanged indicates that LBNP reactions in space flight can be evaluated using the criteria applied on the earth.

[Text] A linear discriminant function was obtained previously [1] for a sample of 25 preflight and 25 postflight observations, which permits calculation of overall digital assessments of reactions to lower body negative pressure (LBNP). This function was used to assess LBNP reactions during spaceflights, when tolerance to tests also remained quite satisfactory. The overall evaluations fluctuated over a rather wide range, but on the whole their distribution was similar to the postflight findings, which can be interpreted as intensification of reaction to LBNP during long-term exposure to flight factors. When interpreting flight data, there is a valid question of whether one can assess inflight LBNP reactions using the same criteria and set of parameters as are used in ground-based studies. We shall discuss this question here on the basis of the results of separate factor analysis of ground and flight data concerning cosmonauts' reactions to the LBNP test.

Methods

Factor analysis is one of the procedures of analysis of variations [2, 3, 5]. Factor analysis is based on the conception that there is a small number of discrete basic parameters or properties underlying the many parameters of a

phenomenon under study or a statistical set of objects that can be measured directly. They characterize the internal structure of the object and determine the significance of observed features. These discrete parameters are called factors. Internal factors cannot be directly measured, but their correlation with the measured tags and contribution to overall dispersion can be assessed. In addition, meaningful interpretation of factors is possible, i.e., a general name has been picked for each factor. For example, in factor analysis of parameters of the cardiovascular system, there can be factors with names such as vascular tonus, condition of the heart, etc. Ultimately, we are dealing with the factor structure of a phenomenon or statistical set of objects.

The intent of using factor analysis in this study was to compare the factor structures of the reaction to LBNP on the ground and in flight. If the same factor structure is retained in flight as on the ground, we are justified in believing that the set of parameters used to assess LBNP reactions and correlations between their mass remain unchanged. If, however, the factor structure would change appreciably, the question arises of correcting the system of ratings developed for conditions on the ground. Using the method of main components, we processed the same material as was used before [1] for discriminant analysis of LBNP reactions. The sample of ground-based studies consisted of 50 cases and of flight studies, 36. Each test was characterized by two absolute parameters (heart rate--HR-- and ejection period--EP) and six differences between values of parameters at rest and during the test (HR, diastolic and pulse pressure (BP_d and BP_p, rate of propagation of pulse wave over vessels of the elastic type--V_e, stroke volume and cardiac output--SV and CO). Standard programs were used for the calculations [4].

Results and Discussion

The Table shows the factor structure of reactions to LBNP on the ground and in flight. The first 3 factors are described, since they together determine about 75% of the overall scatter. In the sampling of ground data, the first factor is closely interrelated with two parameters, changes in SV and CO. The other coefficients of correlation are low or do not reach statistically significant levels. The combination of SV and CO in the first factor allows us to assume that this factor reflects the conditions of formation of cardiac output. The decline of CO during exposure to LBNP can occur with different degrees of decline of SV. Retention of a rather high SV is indicative of relatively good venous return, i.e., optimum conditions for cardiac function. Consequently, we can call the first factor the "factor of venous return." The second factor combines the values of HR and EP. We know that there is a rather close correlation between these parameters. Deviations of EP from "nominal" values for a given pulse rate is usually related to changes in load on the heart and myocardial contractility. Obviously, we can call the second factor the "factor of cardiac state." The third factor is closely related only to changes in BP_p.

According to the flight data, the first factor is also verly closely related to changes in SV and CO. It also demonstrates a high correlation with BP_p changes. The level of the latter parameter depends on several conditions, the main ones being vascular tonus and SV. Consequently, BP_p indirectly characterizes conditions at the cardiac input--venous return. Thus, the

move of BP_p into the first factor does not alter proper interpretation of this factor. The second factor is entirely identical to the one found for ground-based conditions, while the third is closely correlated only with BP_d, i.e., with the characteristic of vascular tonus which was previously reflected in BP_p.

Factor structure of LBNP reaction on the ground and in flight

Where studied	Factor	P,%*	Coefficients of mass with following parameters							
			HR	ΔHR	ΔBP_d	ΔBP_p	ΔV_e	EP	ΔSV	ΔCO
On the ground	First	37	-0,027	0,082	0,305	-0,120	0,238	-0,145	-0,736	0,937
(n 50)	Second	25	-0,772	0,288	-0,118	0,088	0,186	0,939	0,050	0,098
	Third	16	-0,053	0,016	-0,134	0,967	0,199	0,081	0,260	0,043
In flight	First	30	0,129	0,075	-0,079	0,877	-0,059	0,202	0,893	0,605
	Second	27	0,873	0,447	-0,084	0,050	0,048	-0,896	-0,105	-0,211
(n=36)	Third	19	-0,031	0,035	-0,980	0,207	0,134	-0,149	-0,066	-0,075

*Relative contributions to overall scatter.

On the whole, comprehensive analysis of factor structure shows that weightlessness and other specific flight conditions do not cause significant changes in factors determining overall scatter of features of LBNP reaction. The proportion of factor contributions to overall scatter also is virtually the same. Consequently, inflight reactions to LBNP can be evaluated according to the same parameters and criteria as on the ground. This applies, in particular, to overall numerical evaluations obtained with use of the linear discriminant function [1]. As an additional finding, it is noteworthy that, in spite of the possible flaws in the method of calculating SV, this parameter was closely correlated with the first factor. This stresses the paramount significance of venous return to tolerance to LBNP tests.

BIBLIOGRAPHY

1. Voskresenskiy, A. D., Degtyarev, V. A., Doroshev, V. G. et al., KOSMICHESKAYA BIOL., No 4, 1981, pp 4-6.

2. Yeliseyeva, I. I. and Rukavishnikov, V. O., "Logika prikladnogo statisticheskogo analiza" [Logic of Applied Statistical Analysis], Moscow, 1982.

3. Maksimov, G. K. and Sinitsyn, A. N., "Statisticheskoye modelirovaniye mnogomernykh sistem v meditsine" [Statistical Models of Multidimensional Systems in Medicine], Leningrad, 1983.

4. "Sbornik nauchnykh programm na fortrane" [Collection of Scientific Programs in FORTRAN], Moscow, 1974.

5. Kharman, G., "Sovremenyy faktornyy analiz" [Modern Factor Analysis], Moscow, 1972.

UDC: 629.78:612.014.461.3+612.015.31:541.135

EFFECT OF SPACEFLIGHT FACTORS ON HORMONAL REGULATION OF FLUID-ELECTROLYTE METABOLISM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 20 Oct 83) pp 6-8

[Article by V. Yu. Semenov]

[English abstract from source] This paper presents the results of examinations of 19 test subjects exposed to head-down tilting at -8 and -15° and of 14 test subjects kept in water immersion for 24 hours. During the first hours of exposure the renal excretion of water and monovalent ions increased. Renin and aldosterone measurements showed that changes in the sodium and potassium excretion were produced by a lower activity of the renin-angiotensin-aldosterone system in the first 1.5 hour of hypokinesia. During immersion the renal excretion of calcium and magnesium also grew, especially in the evening and at night. The PTH production and calcium concentration in blood increased, thus augmenting the nephron load. The diurenal rhythms of the renal excretion of potassium, calcium and magnesium remained unchanged and those of water, osmotically active substances and sodium varied. The data obtained indicate significant changes in water-salt metabolism and its regulation within the first hours of head-down tilt and water immersion.

[Text] When man is exposed to spaceflight factors there are changes in fluid-electrolyte metabolism and in activity of endocrine glands, which are very important to maintenance of the hydroionic status [1-3, 12]. Most studies pertained only to fluid-electrolyte metabolism or only the hormone status [11, 13]. Attention had been focused on mechanisms of adaptation during long-term exposure to spaceflight factors. At the present time, it is growing very important to investigate fluid-electrolyte metabolism and the systems that control it at the initial stage of adaptation to weightlessness. Studies in this direction will probably establish the pathogenetic mechanisms of alteration of fluid-electrolyte metabolism, which would lead to development of effective preventive methods and agents.

Our objective here was to investigate excretory function of the kidneys and hormonal status of man on the first day of exposure to antiorthostatic hypokinesia (AOH) [head-down tilt] and immersion (IM).

We studied 19 healthy men submitted to AOH (head end of the bed tilted to -8 and -15°), as well as 14 subjects submitted to immersion. The tests began at 0930-1000 hours. Material was collected for 24 h before IM and AOH and for 24 h during these exposures. The subjects were on a standard food allowance and fluid intake.

We analyzed venous blood and urine, which was collected periodically at very strictly determined times of day. We assayed sodium and potassium of blood serum by flame photometry, calcium by titration, magnesium by the method of atomic absorption flame spectrophotometry, creatinine by spectrophotometry using the Jaffe reaction with picric acid and osmotically active substances by the cryoscopic method. Hormonal status was examined on the basis of assaying blood levels of the following hormones: renin, aldosterone, adrenocorticotropic (ACTH), parathyroid (PTH) hormones and cortisol; for this purpose we used the radioimmune method with test sets. The samples were counted on a gamma counter. In analyzing the obtained data, we compared fractions referable to the same time of day. The results were submitted to processing by methods of variational statistics.

Results and Discussion

During the first hours of exposure to conditions simulating the physiological effects of weightlessness, there was the most significant increase in excretion of fluid, osmotically active substances, sodium and potassium. It should be noted that under IM conditions excretion of the analyzed substances differed little from background values for the first 1.5 h after immersion (Table 1), whereas under AOH conditions there was increase in this parameter within the first 1.5-3 h (Table 2). However, on the whole the changes in fluid-electrolyte metabolism, as well as in hormonal status, under IM and AOH conditions, at -8 a and -15°, were virtually the same, but somewhat more marked with IM.

Table 1. Excretion in urine of fluid (mℓ/min), osmotically active substances (μosmol/min), sodium and potassium (μeq/min) before and on first day of immersion

Time of study	Fluid		Sodium		Potassium		Osmotically active substances	
	BG	IM	BG	IM	BG	IM	BG	IM
1130	1,34±0,20	1,35±0,19	119±15,3	121±15,0	60±9,1	68±10,1	746±69,1	796±64,6
1500	0,83±0,04	2,08±0,30**	141±15,1	237±37,7*	44±4,2	81±12,7*	729±62,1	1070±122,4*
1900	1,11±0,12	1,59±0,27	156±23,8	274±49,7*	48±5,1	53±12,1	816±92,9	1081±183,6**
2300	0,86±0,08	1,59±0,16**	154±26,1	293±28,2**	37±3,6	53±8,5	849±111,0	1242±151,5**
0700	0,69±0,09	0,71±0,04	68±11,6	114±5,5**	19±4,1	25±2,5	523±82,8	610±39,4*

Note: Here and in Tables 2-4, one asterisk indicates $P<0.05$ in relation to background and two, $P<0.01$.

Key: BG) background [here and in Table 2]

Table 2. Excretion in urine of fluid (mℓ/min), sodium and potassium (μeq/min) before and on first day of AOH

Time of study	Fluid		Sodium		Potassium	
	BG	AOH	BG	AOH	BG	AOH
1300	0,94±0,07	1,46±0,37*	152±12,3	189±38,1*	74±5,9	83±15,5
1800	1,20±0,08	1,37±0,14	195±14,2	228±25,3*	68±8,1	69±7,2
2300	1,05±0,17	1,15±0,19	164±21,5	209±40,2*	45±6,0	42±13,2
0800	0,73±0,09	0,77±0,08	101±15,7	153±22,4	33±4,1	31±3,7

Table 3. Blood hormone concentrations before and on 1st day of IM and AOH (-15°)

Hormone	Load	Background	Time of study, hours		
			1.5	5	24
Renin, ng/mℓ/h	IM	2,33±0,27	1,58±0,25*		1,99±0,31
	AOH	2,41±0,18	0,73±0,16*	0,74±0,20*	3,97±1,30
Aldosterone, pg/mℓ	IM	82±13,6	78±8,1		84±16,2
	AOH	55±15,5	11±10,0*	2±0,70*	144±28,2
ACTH, pg/mℓ	IM	14,3±1,71	14,4±1,24		11,4±1,81
	AOH	23,0±4,00	19,3±9,29	16,4±7,95	12,6±0,96
Cortisol, ng/mℓ	IM	148±23,3	154±24,4		188±31,5
	AOH	140±83,5	198±51,1	53±8,3	256±24,5
PTH, ng/mℓ	IM	0,88±0,15	1,13±0,19*		1,08±0,12

Concurrently with increase in renal excretion of sodium during AOH, already in the first 1.5 h after starting the experiment there was decline in blood renin and aldosterone levels (Table 3). With exposure to IM, blood aldosterone concentration virtually failed to differ from the base value for the first 1.5 h after immersion, and this was consistent with changes in excretion of sodium in urine.

Analogous changes had been demonstrated previously, and they had been attributed primarily to diminished activity of mineralocorticoids and ADH due to change in afferent impulsation from volumoreceptors and baroreceptors of the atria and low-pressure vessels [6, 9, 10].

In addition to increase in excretion of fluid and monovalent ions in the tests with IM, there was increased excretion of calcium and magnesium, which reached maximum values in the evenings (Table 4). At the same time, there was an increase in blood calcium content, to 4.6±0.12 meq/ℓ, versus 4.0±0.22 meq/ℓ in the background period, which led to a greater load on the nephron and, perhaps, stimulation of synthesis of thyrocalcitonin [7], which diminishes calcium reabsorption in the renal tubules [5, 8]. The increase in blood calcium concentration was apparently related to increased PTH production, a higher level of which had been demonstrated in blood as early as 1.5 h after submersion in the immersion medium (see Table 3). Under these conditions, the increased PTH production could have been related to the body's stress reaction to unusual living conditions [14]. However, an increase in blood ACTH and cortisol content, which is inherent in adaptation reactions, was not always demonstrable

(see Table 3). It should be noted that, not infrequently, we observed dissociation between changes in blood ACTH and cortisol concentrations. Analogous dissociation had been demonstrated in a postflight testing of cosmonauts [12], which suggested inadequate increase in ACTH activity and intensification of its extraadrenal action [4].

Table 4. Excretion in urine of calcium and magnesium (μeq/min) before (I) and on 1st day (II) of immersion

	Period of study	Time of study				
		1130	1500	1900	2300	0700
Calcium	I	5,9±0,92	11,6±1,87	10,7±1,71	12,9±3,18	6,9±1,14
	II	7,3±1,18	10,7±1,28	12,8±2,03	16,5±2,75	8,6±1,48
Magnesium	I	4,7±0,52	7,0±0,84	7,2±1,22	8,0±1,31	5,1±1,19
	II	5,1±0,68	6,1±0,93	8,7±1,61	10,6±1,05	8,0±1,17*

Thus, the change to IM and AOH conditions is associated with increase in renal excretion of fluid, osmotically active substances, sodium and potassium in the morning and daytime, as well as calcium and magnesium in the evening and nighttime hours of the first day of the study. This is associated with a change in circadian rhythm of excretion of fluid, sodium and osmotically active substances. The demonstrated changes in fluid-electrolyte metabolism are largely attributable to diminished activity of the renin-angiotensin-aldosterone system, changes in activity of glucocorticoids and increase in PTH concentration in blood serum.

BIBLIOGRAPHY

1. Balakhovskiy, I. S. and Natochin, Yu. V., "Obmen veshchestv v ekstremal'nykh usloviyakh kosmicheskogo poleta i pri yego imitatsii" [Metabolism Under the Extreme Conditions of Real and Simulated Spaceflights], Moscow, 1973.

2. Gazenko, O. G., Grigor'yev, A. I. and Natochin, Yu. V., KOSMICHESKAYA BIOL., No 5, 1980, pp 3-10.

3. Grigor'yev, A. I., "Regulation of Fluid-Electrolyte Metabolism and Renal Functions in Man During Spaceflights," author abstract of doctoral dissertation, Moscow, 1980.

4. Noskov, V. B., Balakhovskiy, I. S., Grigor'yev, A. I. et al., KOSMICHESKAYA BIOL., No 1, 1981, pp 29-32.

5. Agus, Z. S., Wasserstein, A. and Goldfarb, S., ANN. REV. PHYSIOL., Vol 43, 1981, pp 583-595.

6. Ammons, W. S., Santiesteban, H. L., Koyama, S. et al., AM. J. PHYSIOL., Vol 239, 1980, pp H342-H348.

7. Copp, D. H., J. ENDOCR., Vol 43, 1969, pp 137-161.

8. "Calcium, Phosphate and Magnesium Metabolism. Clinical, Physiologic and Diagnostic Procedures," ed. B. E. C. Nordin, Edinburgh, 1976.

9. Goetz, K. L., Bond, C. C. and Bloxham, D. D., PHYSIOL. REV., Vol 55, 1975, pp 157-205.

10. Gauer, O. H., in "The Kidney and Liver Disease," ed. M. Epstein, New York, 1978, pp 3-17.

11. Epstein, M., DeNunzio, A. G. and Ramachandran, M., J. APPL. PHYSIOL., Vol 49, 1980, pp 184-188.

12. Leach, C. S., ACTA ASTRONAUT., Vol 6, 1979, pp 1123-1135.

13. Leach, C. S. and Rambaut, P. S., in "Biomedical Results From Skylab," ed. R. S. Johnston, L. F. Dietlein, Washington, 1977, pp 204-216.

14. Schneider, A. B. and Sherwood, L. H., METABOLISM, Vol 23, 1974, pp 975-1007.

UDC: 629.78:[612.124:547.466.25]-06:613.21

EFFECT OF SPACE DIET ON BLOOD VALINE CONTENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 19 Dec 83) pp 8-19

[Article by I. G. Popov and A. A. Latskevich]

[English abstract from source] The content of valine was measured in plasma of 6 healthy male test subjects who were either on a normal or Salyut-5 space diet for 30 days. The measurements were performed with the aid of a Hitachi KLA-3B amino acid analyzer. Unlike other studies, blood samples were drawn every 5 days. The results suggest that the postflight decrease of the valine content is associated with the food composition. This makes it necessary to improve the amino acid composition of space diets and the technology of their manufacture. The foodstuffs used in the recovery period should be supplemented with amino acids, particularly valine, to compensate for enhanced anabolic processes.

[Text] Investigation of free amino acid levels in blood plasma of cosmonauts after completion of missions revealed changes in concentrations of a number of amino acids, as compared to preflight status [7, 8, 12, 19]. The demonstrated changes were due to the effect of the set of spaceflight factors, including the specific diet.

Among the essential amino acids, a decline in concentration of which was noted after missions, valine (α-aminoisovalerianic acid referable to nonpolar or hydrophobic amino acids) merits serious attention; one can assess the body's supply of nutritional protein from its level in plasma [13, 18].

It is interesting to test the effect of cosmonauts' diets on plasma valine content without the concurrent effect of other flight factors.

We report here the results of a study of plasma valine content in male subjects given the space diet developed for the crews of Salyut-5 for 30 days.

Methods

In the base period, the subjects were on an individual, unregulated diet; then, for 30 days (experimental period) they were given the standard daily food

allowance for cosmonauts, which had been used in the missions aboard Salyut-5 spacecraft (first and second missions). The schedule called for three meals. A mandatory condition was to consume all of the food offered. We used six variants of daily diets that made it possible to schedule meals on a 6-day menu. After staying on the space diet for 30 days, the subjects again changed to individual, unregulated diet (recovery period). At all stages of the study, the subjects performed their customary work within the limits of occupational group I of physiological dietary standards of the Institute of Nutrition, USSR Academy of Medical Sciences, set in 1982 (2700-2800 kcal or 11,715-11,297 kJ). Thus, in the course of testing plasma valine content, there was change only in the diet, while living conditions were virtually unchanged.

A total of 6 healthy men 18 to 40 years of age participated in the studies.

Venous blood samples were drawn in the mornings, on a fasting stomach, every 5 days, which distinguished this investigation from most others, when blood was taken considerably less often.

We also assayed valine and threonine content of the foods in all 6 diets of the Salyut-5 crews.

Blood samples were prepared for analysis by the standard method [7, 8, 12, 15]. Valine content of plasma and foods was determined using a KLA-3B automatic amino acid analyzer of the Hitachi firm.

Nutritional value of the daily food allowance of cosmonauts, which we used in our studies, was as follows: 98 g protein, 137 g fat, 317 g carbohydrate, with an energy value of about 2980 kcal (estimates for the assimilated part of the food allowances).

Results and Discussion

In the base period, during their routine activities and on their usual individual diets, plasma valine content was in the range of 1.93-2.52 mg% in all 6 subjects, the mean concentration being 2.35±0.09 (Table 1). The demonstrated concentrations correspond to the physiological fluctuations of this amino acid in blood, which are cited in the "Great Medical Encyclopedia" (BME), 3d edition [1] as the "approximate data for adults." It should be noted that this BME "norm" was obtained on the basis of generalization of the data of a number of authors who tested men and women of different ages in diverse occupations, whose diets were different, and nonidentical investigative methods and equipment had been used. For this reason, it is not surprising that a rather wide range of fluctuations of valine concentration is suggested as the norm, with a 1.5 mg% range (see Table 1). Such a wide range of concentrations is indicative, in particular, of significant variability of alimentary protein supply in the body, primarily animal protein. The subjects also presented significant fluctuation of plasma valine concentration due to dissimilar intake in food, its individual metabolism and reserve of this amino acid in the body. However, the range of fluctuations of valine concentration in the subjects was still noticeably narrower than would follow from the data cited in BME [1].

Table 1. Valine concentration in plasma of subjects, Salyut-5 crew members, as well as individuals of different ages and occupations according to data of several authors

Individuals tested	Valine, mg%	Data from literature	Valine, mg%	Dynamics of fluctuations
Subjects:				
A-v	2.44	I.S.Balakhovskiy[1]	1.5-3.0(2.25)	1.5
N-v	2.52	G. Muller [17]	1.36-2.66(1.99)	1.3
L-ch	2.34			
M-n	2.53	D. Dimmer [14] and		
		N.V. Semenov [11]	2.37-3.71(3.04)	1.34
K-v	2.38			
Sh-s	1.93			
Group mean (M±m)	2.35±0.09	B.I.Zbarskiy, N.I. Ivanov and R.R. Mardashov [3]	2.2-3.2 (2.7)	1.0
		S.Moore and W. Stein [16]	2.88	
fluctuations:		N.N.Pushkina [10]		
degree	0.59	& I.B.Zbarskiy [4]		
range	1.93-2.52	A.S.Ushakova and T.F.Vlasova [19] (n=80)	2.54±0.06	
Salyut-5 crew, pre-flight: first		Our data [9] (healthy adult		
mission [7]--CDR	2.80	males, n = 124)	2.33±0.02	
FLE	2.06			
second mission [8]				
CDR	2.22			
FLE	2.71			
cosmonaut group (n = 4), range of fluctuations	2.06-2.80 (2.45)			
degree of fluctuat.	0.74			

Plasma valine levels in the base period were also in the physiological range cited for healthy males in the manual of G. Muller [9], who gives a somewhat narrower range of concentrations than indicated here and a lower bottom of the normal range. Judging from the physiological standards suggested by a number of other authors [3, 11, 14], valine concentration was below the bottom of the physiological range in only 1 of our subjects (Sh-s). There was also a subject (L-ch) with plasma valine concentration close to the bottom of the normal range. If we were to be guided by the mean values suggested previously [4, 10, 16], all of the subjects had lower than normal concentrations of valine in the base period. According to A. S. Ushakov and T. F. Vlasova [19], who tested valine in 80 healthy males by a method identical to ours, plasma valine content was below the mean in 4 subjects. Previously, in a screening of 124 healthy men, we established a mean valine concentration of 2.33±0.02 mg% [9], i.e., somewhat lower than the means cited in [4, 10, 16, 19],

but within the range of physiological fluctuations cited in [1, 11, 14, 17]. A comparison to our physiological norm revealed that plasma valine content in the base period was relatively low in only one subject (Sh-s), normal in 1 subject (L-ch) and somewhat above normal in 4 subjects. On the whole, however, for the group, the mean indicators of plasma valine content were very close to the levels we previously found in a screening of 124 healthy men 18 to 45 years old under ordinary living conditions, in a temperate climate zone and with unregulated diet [9].

Thus, in the base period, plasma valine content was within the physiological range in most subjects, but the greater part of them presented a level that was slightly below the mean "norm." Valine concentration in plasma could be assessed as somewhat low in only one subject (Sh-s) [3, 4, 9, 10, 11, 14, 16].

Analysis of plasma of the crew of Salyut-5 during the period of preflight training revealed that valine content was higher in two cosmonauts than in all of the subjects in the base period and in the two others, lower than in most of our subjects (see Table 1). The range of fluctuations of valine concentrations in this group of cosmonauts (n = 4) was wider than in our subjects in the base period, in spite of the fact that it would appear the cosmonauts had more homogeneous living conditions and diet than our subjects.

Table 2 lists the results of assaying plasma valine content in our subjects on the 5th, 10th, 15th, 20th, 25th and 30th days of using the Salyut-5 space diet, with retention of ordinary living conditions on the ground.

On the 5th day of the test period, 2 subjects presented elevation and 2 others decline of plasma valine concentration. In the other 2 subjects, the concentration remained at virtually the base level (if we proceed from the fact that the method had a margin of error of ±2%). The range of fluctuations of concentrations in the group as a whole broadened due to changes in concentrations in both the direction of decrease and increase. Mean plasma valine concentration for the group of subjects showed virtually no change (-2.13%).

The next time blood was drawn, on the 10th day of the space diet, 2 subjects showed lower plasma valine concentration and 1, higher than in the base period. It remained virtually at the initial level in the remaining 3 subjects although there was a general tendency toward decrease in concentration of this amino acid. As compared to the status on the 5th day, 4 subjects presented a tendency toward further decline of plasma valine. However, the concentration of valine increased to the base level and became more "favorable" than on the 5th day in 1 subject (Sh-s).

Analysis of the dynamics of plasma valine content in the base period and on the 5th and 1st days of the test period leads us to conclude that there was ± fluctuation of valine concentration in at least half the subjects (A-v, N-v, K-v) in relation to the base status. Only 1 subject (L-ch) revealed a progressive decline of valine level on the 5th and 10th days of intake of the space diet. In the group as a whole, the fluctuations of plasma valine concentration and their range on the 10th day were virtually the same as in the base period, but somewhat less marked than on the 5th day of the test period. Due to the tendency toward decrease in valine concentration in most subjects, its mean (M) on the 10th day dropped somewhat, as compared to the base period and 5th day of experimental diet.

Table 2. Plasma valine content in subjects on usual diet and with 30-day use of space diet on the ground

Subject	Base period (usual diet)	Period of intake of space diet, days												Individual fluctuations over 30-day period	Degree of individual fluctuations	Individual mean over 30-d period (M±m)
		5		10		15		20		25		30				
		plasma valine content														
		mg%	% of base level	mg%	% of base level	mg%	% of base level	mg%	% of base level	mg%	% of base level	mg%	% of base level			
A-v	2,44	2,39	—2,05	2,51	+2,86	2,40	—1,64	2,36	—3,28	2,30	—5,74	2,32	—4,92	2,30—2,51	0,21	2,38±0,03
N-v	2,52	2,61	+3,57	2,48	—1,60	2,34	—7,14	2,39	—5,16	2,30	—8,74	2,27	—9,92	2,27—2,61	0,34	2,40±0,05
L-ch	2,34	2,07	—11,54	1,97	—15,81	1,76	—24,79	1,80	—23,08	2,14	—8,55	2,18	—6,84	1,76—2,18	0,42	1,99±0,06
M-n	2,53	2,50	—1,20	2,48	—2,00	2,64	+4,34	2,31	—8,70	2,36	—6,72	1,41	—44,27	1,41—2,64	1,23	2,28±0,18
K-v	2,38	2,48	+4,20	2,27	—4,62	2,33	—2,10	2,51	+5,46	2,33	—2,11	2,21	—7,15	2,21—2,51	0,30	2,35±0,04
Sh-s	1,93	1,76	—8,81	1,92	—0,52	2,74	+41 96	1,92	—0,52	1,90	—1,56	1,81	—6,22	1,76—2,74	0,98	1,99±0,12
Entire group: range of fluctuat.	1,93—2,53	1,76—2,61		1,92—2,51		1,76—2,74		1,8—2,51		1,9—2,36		1,41—2,32		1,41—2,74		
degree of fluctuat.	0,60	0,85		0,59		0,98		0,71		0,46		0,91			1,33	
mean	2,35 ±0,09	2,30 ±0,13		2,27 ±0,11		2,36 ±0,17		2,21 ±0,12		2,22 ±0,07		2,03 ±0,14				

On the 15th day on the space diet, 2 subjects presented lower plasma valine level than in the base period, 2 had a higher level, and 2 showed virtually no change. We were impressed by the fact that continuing decrease in valine concentration on the 15th day was found in only 1 subject (L-ch). Continuous increase in valine content of plasma was not demonstrable in any subjects. In one case (Sh-s), where there was a relatively low valine concentration in the base period, as well as on the 5th and 10th days of space diet, it increased drastically on the 15th day (by 42%) and reached normal value according to [1, 3, 9, 11, 14, 17, 19]. On the whole for the group, mean valine concentration was virtually restored to the base level. There were more marked fluctuations of valine concentration and the range was broader on the 15th day of the test period than in the base period and on the 10th day of space diet, but corresponded approximately in range of fluctuations to the 5th day of the experimental period.

On the 20th day of the test period, plasma valine concentration was lower in 4 subjects than in the base period, it was higher in 1 case and remained at virtually the base level in another. As compared to the status on the 15th day, valine concentration decreased in half the subjects and increased in the other half. In only 1 subject (L-ch) valine content was below the base level on the 20th day, as it was on the 5th, 10th and 15th days. In another case (Sh-s), after the increase in valine concentration on the 15th day to the normal mean values according to [1, 3, 4, 9, 10, 16, 19], there was another decline on the 20th day to the base level, which had been low. The range of fluctuations in valine levels on the 20th day was somewhat broader than in the base period and on the 10th experimental day due to lowering of the bottom limit of concentrations. However, it was narrower than on the 5th and, particularly, 15th day of the test period. Mean concentration of valine in the group as a whole was lower than in the base period or on the 5th, 10th and 15th days of the test diet. Thus, in the group of subjects as a whole, there was a more marked tendency toward decrease in plasma valine concentration on the 20th day of the space diet.

On the 25th day of the space diet, plasma valine concentration was below the initial level in 5 out of 6 subjects and almost corresponded to the initial status in 1 subject (Sh-s) with, however, a tendency toward decline. It should be noted that this subject continued to have a relatively low plasma valine level. In 1 case (L-ch), valine level improved somewhat, as compared to the status on the 5th, 10th, 15th and 20th days. The range of fluctuations in valine concentrations for the group of subjects as a whole became narrower than in the base period and status on the 5th, 10th, 15th, 20th days of the test period, due to predominant decline of the top of the range of fluctuations. Mean valine concentration in the group of subjects was lower than in the base period and on the 5th, 10th and 15th days of space diet. On the 30th day of the space diet, the general tendency toward decrease in plasma valine content was still present and even became more marked. Plasma valine concentration was lower in all six subjects than in the base period. Mean valine concentration for the group of subjects was 13.6% lower than in the base period, and this was the lowest in the test period. The range of fluctuations of valine concentrations was wider than in the base period, with a shift in the direction of decline in absolute concentrations.

Plasma valine concentration remained within the range of physiological fluctuations [1, 17] in all 6 subjects during the 30-day period of our study. At the same time, judging by the "norm" cited in [3, 4, 9-11, 14, 19], plasma valine content was low in 2 subjects on the 5th and 10th days, and more so than in the base period.

On the 15th day, valine concentration was lower than cited in [3, 11, 14] in only 1 subject. At this time, all subjects had a valine concentration that was below the mean "norm" according to [4, 10, 16], but this applied to only 4 of them according to [1]. According to our data [9], valine concentration was appreciably lower than the mean in only one subject.

According to the standards cited in [11, 14], plasma valine concentration on the 25th and 30th days of the test period was below the bottom of the range of physiological fluctuations; however, according to [3], this was observed in only 2 cases (L-ch, Sh-s) on the 25th day and 3 on the 30th day. According to mean valine concentration [4, 10, 16, 19], it was low in all subjects. According to [1, 9], there was a low valine level on the 25th day in 2 subjects and according to [17], in 1 out of the 6 subjects. On the 30th day, valine content was low in 4 subjects according to the data in [1] and in 2 out of 6 according to [17]. According to our data [9], plasma valine was somewhat lower than the mean values on the 30th day in 5 out of 6 subjects.

Let us refer to the dynamics of plasma valine content in our group of subjects (n = 6) as a whole and in each of them individually.

Mean plasma valine concentrations in the group as a whole (M±m) had a tendency toward decline in the course of the 30-day period, particularly in the second half of the period of intake of the space diet. This parameter was lowest on the 30th day.

The individual mean concentration of valine decreased, as compared to the base status, but insignificantly in 4 out of 6 subjects (A-v, N-v, L-ch, M-n) on the 30th day of the test period. In the other two it remained at virtually the initial level. It should be noted that subject Sh-s, who presented the relatively lowest plasma valine content in the base period, which could be rated as low according to most cited authors [1, 3, 4, 9-11, 14, 16, 19] and indicative of inadequate valine supply in the body throughout the test period, with the exception of the 15th day, continued to show a low level of this amino acid in plasma. On the 5th and 30th days, there was a tendency toward further decrease in valine concentration. The mean 30-day concentration was generally close to the base status, mainly due to increase in concentration of this amino acid to a normal level on the 15th day according to the standards cited by most authors [1, 3, 4, 9, 10, 11, 14, 16, 17, 19]. The demonstrated increase in valine could have been due to intensification of processes of reutilization and redistribution of valine supply in the body in order to normalize the share of this amino acid in the plasma pool of free amino acids.

In all of the subjects, the fluctuations in concentration of valine (individual fluctuations of plasma valine) were less significant in range over the entire 30-day period than for the group of subjects as a whole. The degree of individual fluctuations of valine concentration was less marked than for the group

as a whole (see Table 2). Individual mean concentrations of valine in this period were higher in four subjects than the mean valine concentration for the group as a whole and they were lower in two subjects. It should be noted that the range of fluctuations in valine concentration was relatively wider in subject Sh-s than in the other subjects due to the increase on the 15th day and in subject M-n due to drastic decrease in valine concentration on the 30th day. In most subjects, the range of fluctuations of individual concentrations of valine was small. Thus, individual fluctuations of valine concentration were less significant than in the group as a whole, which is indicative of the substantial influence of individual distinctions of valine metabolism and its resources in the body on concentration of this amino acid in blood plasma, even when the diet is identical in composition. Of course, living conditions, physical and neuropsychic loads were not entirely identical in this study, and this could also have been of some significance.

During the period of 30-day use of identical food allowances, we could have expected some equalization of plasma valine concentrations in all subjects, as compared to the wider scatter of concentrations in the base period, when individual diet was not regulated. However, the findings as to fluctuation of valine concentrations in the group of subjects as a whole in the course of the test period do not confirm such an assumption. The range of fluctuations in valine concentrations was even broader on the 5th, 15th, 20th and 30th days of the test period than in the base period.

Juging from the initial amino acid status of the subjects, they had started the test period with dissimilar plasma valine content, which could have been a reflection, in particular, of difference in valine supply in the body due to individual dietary differences. Among the subjects, 2 presented a relatively higher plasma valine concentration--Ma-n 2.53 mg% and Nov-v 2.52 mg%. By the end of the 30-day period, their valine concentration decreased by 44.3 and 9.9%, respectively, i.e., to a greater extent than in the other subjects. The decline in valine concentration, as compared to the base period, was demonstrated on the 20th, 25th and 30th days in subject Ma-n and on the 15th, 20th, 25th, 30th days in Nov-v.

In the base period, 3 subjects presented the following mean levels of plasma valine: A-v 2.44 mg%, Kor-v 2.38 mg%, La-ch 2.34 mg%. By the 30th day, the decline in plasma valine concentration in this group constituted 4.9, 7.1 and 6.8%, respectively, i.e., it was somewhat less marked than in the preceding subgroup. A decline in valine concentration, in comparison to the base status, was demonstrated in A-v on the 20th, 25th and 30th days, in Kor-v on the 30th day and in La-ch on the 5th, 10th, 15th, 20th, 25th and 30th days. At other tested times, the changes were in different directions or insignificant.

In subject Sh-s, who presented the lowest valine concentration in the base period, the decline in concentration reached 6.2% on the 30th day, i.e., it was close to the values for the second subgroup of subjects. A substantial decrease in concentration, in comparison to the base status, was noted only on the 5th and 30th days.

The above-described dynamics of individual fluctuations of plasma valine content were apparently attributable to processes of adaptation of protein and amino

acid metabolism to altered nutrition. Against the background of a general tendency toward decrease in plasma valine content due to change in the diet, there were periodic increases in its concentration due to mechanisms of endogenous redistribution of valine resources and more intensive utilization. In subjects with a higher valine supply in the base period, we demonstrated a tendency toward more appreciable decrease in its concentration at the end of the 30th day of the test period. In subjects with relatively lower base supply of valine in the body, the process of adaptation was associated, in the second half of the test period, with relatively less decrease in plasma valine content. In this group of subjects, processes of reutilization and redistribution of valine resources were apparently more intensive, which was reflected in the more significant fluctuations in valine concentration and range of fluctuations in most subjects in this group. Two subjects (Sh-s and La-ch), who presented the lowest concentrations of valine in the base period, retained the lowest concentrations of this amino acid during the test period in most analyses.

Thus, initial valine supply in the body apparently affected the dynamics of adaptation and concentration with altered diet.

Table 3 lists the results of assaying plasma valine in crew members of the Salyut-5 orbital station before their flights and on the 1st postflight day. The data listed there indicate that there was appreciable decrease in plasma valine content in both participants of the first mission after completion of a 48-day flight. After the second mission, which lasted 21 days, the flight engineer (FLE) also presented a low valine concentration, but in the commander (CDR) the concentration of this amino acid even increased, as compared to his preflight status. It should be noted that there was more significant change in valine concentration in the crew of the first expedition, which could be attributed to its longer duration. With regard to the data referable to the second mission, it should also be borne in mind that the CDR took more food during the flight than the FLE, and it was in excess of the established daily allowances. This is confirmed by data on nitrogen and potassium excretion immediately after the flight [8].

A comparison of the data in Tables 2 and 3 can lead us to conclude that the postflight decrease in plasma valine concentration (percentage) in the crew of the first mission is comparable to the decrease in valine concentration on the 30th day of using the same diet in only 1 subject (M-n). In the rest of the subjects, there was less marked decrease in valine concentration on the 30th day of intake of the space diet on the ground. After completion of the 48-day mission, valine concentration was lower in the FLE than in any of the subjects after 30 days on the same diet on the ground. In the CDR, postflight valine concentration was lower than in 5 out of 6 subjects at the end of the 30-day test period. Plasma valine content on the 20th day of using the space diet on the ground was rather similar in value and direction of changes in 4 subjects to the status of the crew of the second mission of Salyut-5 after completion of a 21-day flight. In the group of subjects as a whole, the change in plasma valine content on the 30th day of intake of the space diet was more appreciable (as percentage) than in the crew of the second mission after a 21-day flight. After the 21-day mission, plasma valine concentration in the cosmonauts was higher than in all 6 subjects on the ground after use of the same diet for 30 and even 25 days. On the 20th day, valine concentration was higher than postflight in the CDR in only 1 subject, but lower than in the FLE (second

mission). On the 5th, 10th and 15th days of the ground-based test period, there was more frequent coincidence of concentrations with the postflight status of the crew (second mission).

Table 3. Plasma valine content in subjects during recovery period and in crew of Salyut-5

Subjects	Base period	30th day of experiment		Recovery period, usual diet, day					
				5			10		
	plasma valine content								
	mg%	mg%	% of base level	mg%	% of base level	% of 30-d level	mg%	% of base level	% of 30-d level
M-n	2,53	1,41	—44,27	2,09	—11,4	+48,2	1,78	—29,65	+26,2
N-v	2,52	2,27	—9,92	2,37	—5,96	+4,4	2,51	—0,40	+10,5
A-v	2,44	2,32	—4,92	2,48	+1,64	+6,9	2,40	—1,64	+3,3
K-v	2,38	2,21	—7,15	2,46	+3,36	+11,6	2,14	—10,1	—6,4
L-ch	2,34	2,18	—6,84	2,00	—14,53	—8,3	2,02	—13,68	—8,7
Sh-s	1,93	1,81	—6,22	1,98	+2,59	+9,4	1,84	—4,67	+1,6
Group as a whole:									
fluctuations	1,93—2,53	1,41—2,32		1,98—2,48			1,78—2,51		
range	0,60	0,91		0,50			0,73		
mean (M±m)	2,35±0,09	2,03±0,14		2,23±0,09			2,11±0,12		
Salyut-5 crew (first mission)		After 48-d flight		7th post-flight day					
CDR	2,8	1,66	—40,7	1,53	—45,4				
FLE	2,06	1,36	—34,0	1,66	—19 42				
Salyut-5 crew (second mission)		After 21-d flight					28th postflight day		
CDR	2,22	2,41	+8,5	2,21	—0,46	—8,3	2,40	+8,1	
FLE	2,71	2,59	—4,5	2,17	—20,0	—16,2	2,24	—17,4	

On the 5th day after returning to ordinary, individual and unregulated diet, most subjects showed an increase in plasma valine concentration, as compared to their status on the 30th and 25th days of using the space diet (see Table 3). In only 1 case (L-ch) did the concentration decrease by 8%, as compared to the 30th day of the test diet. As compared to the base period, valine was lower (by 5.5-14.5%) in 3 subjects, it became even higher (by 2.6-3.4%) in 2 and was virtually restored to the initial level in 1 subject (method's margin of error 2%). Mean concentration for the group of subjects increased, as compared to the status on the 20th, 25th and 30th days of the test diet, but was still lower than in the base period and the first half of the test diet period. The range of concentrations diminished, as compared to the 30th day of the test period, and cameclose to the base status. In all subjects, the concentration of valine was within the normal range of physiological fluctuations cited in [1, 17], but according to the data in [3, 11, 14] this parameter was lower than the bottom of the normal range in 3 subjects. In all of the subjects, plasma valine content was less than the mean values cited in [4, 10, 16, 19]. In our studies [9], valine concentration was below the mean level in only 3 cases.

On the 10th day of the recovery period, valine concentration was higher in 3 out of the 6 subjects than on the 30th day of the test period, it was lower in 2 and on the same level in 1. As compared to the base period, valine concentration was lower in 4 subjects and remained virtually on the same level in 2. Mean valine concentration for the group as a whole was higher than on the 30th day of the test period, but did not reach the base level. In all cases, plasma valine content was within the range of physiological fluctuations according to [1, 17], but below it in 4 subjects according to [10, 3, 11, 14]. In all 6 subjects, valine concentration was below the mean values cited in [4, 10, 16, 19] and in 4 out of the 6 subjects it was below our previous data [9].

On the 7th day after the 48-day flight aboard Salyut-5 (first mission), valine concentration decreased even more in the CDR, whereas in the FLE, on the contrary, it increased somewhat, as compared to his status on the first day after landing, but in both crew members it was below the preflight level. As compared to the valine concentration in our subjects on the 5th and 10th days of the recovery period, the CDR and FLE had a lower plasma valine content on the 7th postlfight day in absolute terms, and somewhat different percentile value from their base state. In the crew of the second Salyut-5 mission, plasma valine concentration on the 7th postflight day decreased from the status demonstrated immediately after landing. In the CDR, the valine concentration returned to its preflight level, whereas in the FLE it was even lower than preflight.

On the 28th day, both crew members of the second mission showed an increase in valine, as compared to the 7th postflight day, and the concentration was even greater than preflight in the CDR. We can attribute such dynamics of plasma valine levels in cosmonauts after flights to intensification of anabolic processes in the nature of recovery due to readaptation to conditions on the ground (primarily on the part of the muscular system), which is associated with increased utilization of valine from the reserves of blood plasma. For this reason, preventive measures might be beneficial here in the direction of enriching the recovery diet with valine-containing proteins.

Table 4 lists the results of assaying the essential amino acids, valine and threonine, in 6-day food allowances of comsonauts which, in accordance with the 6-day menu plans, were used to feed our subjects during the 30-day test period and by the cosmonauts during missions aboard Salyut-5. Valine and threonine levels in daily food allowances conformed to or exceeded the adult daily requirements according to the formula for balanced diet [6]. We should mention that there was considerable fluctuation in amounts of these amino acids in the daily food allowances (particularly diet No 2 and No 3). In addition, the correlation between threonine, taken as 1, and valine did not conform to the optimum recommended in the FAO [Food and Agriculture Organization, WHO] standard (particularly in diets No 5 and No 6).

Valine and threonine content was higher in the diet than other recommended physiological standards [2, 5] listed in Table 4. Their levels were somewhat below the ones cited by K. P. Petrovskiy [5] only in diet No 2.

Table 4. Amino acid (valine and threonine) content of daily food allowances of Salyut-5 crew members and test subjects, as well as physiological standard requirements

Amino acid in 24-h food allowance of Salyut-5 crew	Diet						
	№ 1	№ 2	№ 3	№ 4	№ 5	№ 6	$M \pm m$
Valine, g	4,71	3,26	7,85	4,34	5,12	5,23	5,08±0,62
Threonine, g	6,46	2,63	6,92	3,38	5,24	5,77	5,06±0,69
Valine/threonine	0,73	1,24	1,14	1,28	0,95	0,91	1,0

Notes: 1. The FAO standard for adults [5]: valine 1.5 and threonine 1.0.
2. Recommended quantities that reliably provide for nitrogen equilibrium [2]: valine 1.60 and threonine 1.00.
3. The lowest quantity, with which nitrogen equilibrium is obtained [19]: valine 0.40-0.80 and threonine 0.30-0.50.
4. Requirements according to K. S. Petrovskiy [5]: valine 3.8, threonine 3.5.

Thus, while valine content was rather high in the 24-h food allowance of our subjects and cosmonauts, there was a decline of plasma valine level. There may be several causes for this phenomenon: relatively higher protein and valine content in the initial diet, decreased intake of valine from the intestine due to poorer digestibility of proteins and less accessibility of valine for assimilation because of the technology of processing space diets, poorer absorption of valine from the intestine because of its imbalance with other amino acids.

In the case of the ground-based study, the inadequate energy value of the diet as a whole could have played an additional role, since it should have led to increased utilization of amino acids for energy purposes.

A more substantial decline of valine was demonstrated in the spaceflights aboard Salyut-5 than in the ground experiment, which is indicative of presence of additional inflight factors affecting amino acid metabolism, other than the nutritional factor.

The diet for postflight recovery nutrition also merits further improvement with due consideration of the increased amino acid requirements to provide for intensive anabolic processes during readaptation to earth's gravity and intensification of general load on the muscles.

The results of our study warrant the conclusion that the alimentary factor, due to the nature of preflight and inflight nutrition, could play some part in the genesis of decrease in plasma valine content in cosmonauts. For this reason, improvement of amino acid composition of flight diets with respect to both quantity of valine and (perhaps to an even greater extent) its balance with other amino acids and increased accessibility of valine to assimilation in flight should have a positive preventive effect. The latter will require improvement of technology of processing foods for cosmonauts. The requirement of adequate diets with respect to energy is also important.

BIBLIOGRAPHY

1. Balakhovskiy, I. S., in BME [Great Medical Encyclopedia], Moscow, 3d ed., 1980, Vol 12, pp 108-109.

2. Berezov, T. T. and Korovkin, B. F., "Biologicheskaya khimiya" [Biological Chemistry], Moscow, 1982, p 437.

3. Zbarskiy, B. I., Ivanov, N. I. and Mardashev, S. R., Ibid, Leningrad, 5th ed., 1972, p 480.

4. Zbarskiy, I. B., in BME, Moscow, 3d ed., 1974, p 1103.

5. Petrovskiy, K. S., "Gigiyena pitaniya" [Hygiene of Nutrition], Moscow, 2d ed., 1975, p 33.

6. Pokrovskiy, A. A., ed., "Khimicheskiy sostav pishchevykh produktov" [Chemical Composition of Foodstuffs], Moscow, 1976, p 8.

7. Popov, I. G. and Latskevich, A. A., KOSMICHESKAYA BIOL., No 2, 1982, pp 14-19.

8. Idem, Ibid, No 1, 1983, pp 15-20.

9. Idem, Ibid, No 3, 1984, pp 25-34.

10. Pushkina, N. N., "Biokhimicheskiye metody issledovaniya" [Biochemical Investigation Methods], Moscow, 1963, p 349.

11. Semenov, N. V., "Biokhimicheskiye komponenty i konstanty zhidkikh sred i tkaney cheloveka" [Biochemical Components and Constants of Human Fluids and Tissues], Moscow, 1971, pp 26-27.

12. Ushakov, A. S., Vlasova, T. F., Miroshnikova, Ye. B. et al., KOSMICHESKAYA BIOL., No 1, 1983, pp 10-14.

13. Vysotskiy, V. G., Vlasova, T. F., Ushakov, A. S. et al., VOPR. PITANIYA, No 2, 1974, pp 16-19.

14. Dimmer, D. S., ed., "Body Fluids," Washington, 1961 (quoted in Semenov, N. V., "Biokhimicheskiye komponenty i konstanty zhidkikh sred i tkaney cheloveka," Moscow, 1971, p 25).

15. Gerritsen, T., Rehberg, M. L. and Waisman, H. A., ANALYT. BIOCHEM., Vol 11, 1965, pp 460-466.

16. Moore, S. and Stein, W., J. BIOL. CHEM., Vol 211, 1954, p 915.

17. Muller, G., "Clinical Biochemistry and Laboratory Diagnostics," Iena, 1977, p 166.

18. Swendseid, M. E., Tattle, S. G., Figueroa et al., J. NUTR., Vol 88, 1966, pp 239-248.

19. Ushakov, A. S. and Vlasova, T. F., AVIAT. SPACE ENVIRONM. MED., Vol 47, 1976, pp 1061-1064.

UDC: 612.825.8.014.477-064.014.49

OPERATOR'S MENTAL ADAPTATION AND WORK CAPACITY IN SIMULATED WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 18 Nov 83) pp 19-24

[Article by K. K. Ioseliani, A. L. Narinskaya and Sh. R. Khisambeyev]

[English abstract from source] In two head-down tilt studies of 7 and 8 days in duration variations in the work capacity of 24 test subjects were examined and the following stages were distinguished: habituation, stable work capacity, and unstable compensation. Among the test subjects two groups were discriminated: those with plastic and those with inert types of adaptation to a changed environment. It is concluded that the plastic-type people can better and faster adapt to head-down tilt and therefore can work more efficiently during an acute stage of adaptation to weightlessness.

[Text] Assessment of mental work capacity is one of the most important problems of space psychophysiology. This is related to the fact that both the assessment and forecast of mental work capacity based on it have a direct bearing on assuring the safety of spaceflights and reliability of spacecraft crews, particularly during the period of acute adaptation to weightlessness [1].

With reference to work capacity, it should be noted that there is no agreement at the present time concerning guidelines and methods of studying it. Furthermore, there is no specific definition of the very term, "work capacity," which makes it difficult to select adequate measurement methods and criteria for assessing it [3, 13-15, 27]. We construe work capacity to mean the "property of an operator, which is determined by the state of physiological and mental functions and characterizes his ability to perform a specific activity with the required quality and for the required period of time" [22].

Analysis of the literature indicates that there are different methodological procedures, parameters and criteria for evaluating an operator's mental work capacity [7-9, 19]. There has still not been enough work on questions of effects of weightlessness on mental work capacity of operators. The data pertaining to changes in the neuropsychic sphere obtained by most researchers [5, 21, 23, 29-31, 33-35] are qualitative in nature; the methods they used are dissimilar in informativeness and direction, and the subjects they

studied were not referable to homogeneous groups. This presents some difficulties with respect to psychological interpretation of results.

The factual material in the scientific literature [2, 6, 20, 28, 32] indicates that antiorthostatic hypokinesia (AOH) [hypokinesia with head-down tilt] is the best model of the period of acute adaptation to weightlessness under laboratory conditions.

Psychologically, hypokinesia is an example of a "given" regimen by virtue of the need to maintain a horizontal position of the body for a long time. Under such conditions, the mismatch between the customary postural and motor mode and the immobile position of the body during the study [18] is important, and it leads to significant reduction of interoceptive and proprioceptive signaling. As a result, there is development of dysfunction and dystonia, which gradually progress [2, 12, 16].

Since changes in mental work capacity are an inevitable component of the adaptation syndrome [24], it can be assumed that the dynamics of mental work capacity would conform largely to the phases in the period of the body's adaptation to AOH.

We have included here the results of two series of studies involving 24 essentially healthy men: 1st series--AOH for 7 days at an 8° angle of tilt (9 men), 2d series--AOH for 8 days at an 8° tilt (15 men).

To obtain homogeneous, comparable and valid material, we used the 9-point system of rating levels of mental work capacity, which was introduced previously to aerospace practice [7]. By means of integrating the results obtained by different methods, such a system yields reliable quantitative evaluations of levels of mental work capacity in comparable units (points).

Methods*

In selecting the set of methods that permit evaluation of the dynamics of mental work capacity, we took into consideration the breadth of coverage of operator skills that a cosmonaut needs for highly productive work. We used the following methods: 1) "continuous counting at a specified pace," during which we recorded the heart rate (HR), arterial pressure (BP) and respiratory rate (RR) as parameters reflecting the "physiological price" of the work and human psychophysiological reserve capacities. This method permits evaluation of the level of mental work capacity when there is a time limit or shortage, by alternating two opposite work methods; 2) "retrieving numbers with changeovers" (complicated version of "red and black table") to test complex differentiated performance; 3) "cancellation tests" (with interference), which permit testing stability of attention during prolonged monotonous work; 4) "establishing patterns" to assess some aspects of thinking; 5) "compasses" to test capacity to operate with spatial conceptions; 6) "text reproduction" to assess logical memory.

*A detailed description of all of the methods used is given in the book, "Metodiki issledovaniya v tselyakh vrachebno-letney ekspertizy" [Test Methods for Expert Medical Certification of Pilots], Moscow, Voyenizdat, 1972, pp 274-324.

Before starting the test, we trained the subjects using all of the methods in order to develop a stable skill in using them. The tests were performed on the 1st, 3d, 5th and 7th days of AOH, and repeated after AOH.

We obtained an integral evaluation of mental work capacity of each subject using a specially developed formula [11]:

$$J = \frac{\sum_{i=1}^{n} O_i \cdot K_i}{\sum_{i=1}^{n} K_i},$$

where J is integral evaluation, O_i is evaluation using a specific method (grade) and K_i is the weight coefficient of that method.

The choice of weight coefficients (within the limits of a 5-point grading scale) was due to the need for integral determination of subjective (psychological) difficulties of the work and extent of strain on physiological systems involved in the activity. This objectivized the complex rating of mental work capacity. Differentiated analysis of the methods enabled us to assign the appropriate weight coefficients to them: 4 for the method of "continuous counting at a set pace," 3 for "retrieval of numbers with changeover," 2 for "establishment of patterns," 1 for "cancellation test," "compasses" and "reproduction of texts."

Results and Discussion

According to the results obtained in both series of studies, we distinguished stages of breaking in, stable work capacity and unstable compensation in dynamics of work capacity.

Break-in stage (1st-3d day of AOH). In this period there was functional reorganization and establishment of a new dynamic stereotype. Integral rating of mental work capacity dropped in this period by a mean of 0.7-1.7 points, as compared to the background. Speed and sometimes precision of the subjects' action were low in this period, and there was frequent distraction of attention. The subjects had to make a deliberate effort to concentrate. The determining symptoms when the subjects performed given work were a state of somatic discomfort and fluctuations of productivity due to search for the individual optimum mode of performance. This stage was characterized, on the one hand, by "getting accustomed" to the unique living conditions and, on the other hand, emotional elation related to the start of the study.

Stage of stable work capacity (3d-5th days of AOH). At this stage, performance became integral without substantial loss of speed or accuracy in reproducing actions. The integral rating of mental work capacity was higher than at the preceding stage by an average of 0.4-1.2. During this period, by the end of the work day the subjects reported insignificant fatigue, which went away after a night's sleep. The work mode was closest to optimum: efficiency was at a maximum during this period and the results were stable.

Table 1. Comparative mental work capacity of subjects submitted to AOH

Group of subjects	Integral score						t	p
	background	day of AOH				after-effect		
		1	3	5	7			
1	8,3±0,26	7,6±0,32	7,6±0,29	8,8±0,26	8,5±0,24	8,8±0,24	5,68	<0,01
2	7,3±0,31	5,4±0,36	5,8±0,29	6,2±0,28	5,8±0,33	6,8±0,26		

Stage of unstable compensation (6th-8th days of AOH). This stage was characterized by some decline of mental work capacity, as compared to the stage of stable performance (by a mean of 0.3-0.4 points), unstable affect and impaired sleep. The extent of decline of work capacity depended on individual distinctions of the subjects and, for this reason, varied markedly. As a result, on the average for the group, there was merely a tendency toward diminished work capacity, and for this reason this was called the stage of "unstable compensation." In this period, the subjects had a marked feeling of fatigue and changes in some functional parameters (HR, BP, RR). From the standpoint of productivity there was some decrease in speed and accuracy of performance of operations due to increased fatigue, particularly toward the end of the day.

Thus, we could distinguish periods of breaking in, stable work capacity and unstable compensation. In some cases they were very distinct and in others, unnoticeable, discrete. It must be stressed that there was no stage of progressive decline of work capacity, and we failed to observe disorganization of mental performance or refusal to work [4].

The subjects could be divided into two groups according to dynamics of mental work capacity (Table 1): 1) 1st group (14 men, 58% of the subjects), which was characterized by a high stable level of mental work capacity over the entire test period (with a grade of 7.6±0.32 to 8.8±0.26). This group was characterized by easy learning, ability to mobilize in stress-producing situations, good emotional stability and absence of tension when performing their tasks. The dynamics of mental work capacity were characterized by rapid determination of an adequate mode of action, rapid development of skill in the mental task, stability and uniform work pace. In these individuals, the adaptation period ended by the 5th day of AOH. During this time, some subjects observed some slowness of breaking in to the task and diminished capacity for work involving switching attention in the presence of information interference, time limit and shortage. By the 5th day of AOH, mental work capacity of these subjects usually not only returned to the background level, but exceeded it significantly, which was indicative of onset of the stage of stable work capacity (flexible type of adaptation); 2) the subjects of the 2d group (10 men, 42%) were characterized by an unstable level of mental work capacity, fluctuation of quantitative and qualitative parameters of performance of tasks throughout the test period (score 5.4±0.36 to 6.2±0.28). There was decrease in stability of attention, immediate memory and resistance to interference.

During the period of diminished output (stage of unstable compensation), the most diverse errors appeared, which were related to both diminished immediate memory and diminished stability of attention. This group of subjects developed errors of the perseveration type when they changed to the opposite mode of work, and this can apparently be attributed to fatigue that A. A. Ukhtomskiy considered to be the cause of some distinction of the dominant prevailing at a given time [25]. For expressly this reason performance became markedly stereotypic. In some cases there was impaired spatial orientation. In the second group of subjects, unlike the first group, the parameters of mental work capacity were below background values by the end of the AOH period, and they reverted to the base level only after termination of hypokinesia (inert type of adaptation).

Table 2.
Examples of dynamics of number of errors per 100 operations in continuous count at specified pace

Subject	Signal exposure time, s	Background	Day of AOH				After-effect
			1	3	5	7	
V-n (1st group)	2,0	5	8	11	4	3	0
	1,5	13	20	17	9	7	7
S-v (2d group)	2,0	20	28	29	29	25	18
	1,5	28	32	46	48	50	35

As can be seen in Table 2, the subjects in the first and second groups differed in dynamics of errors made when working on "continuous counting at a set pace." It should be mentioned that the first group of subjects made the maximum number of mistakes on the 1st-3d days of AOH, but already by the 5th day performance parameters were above background values. In the second group of subjects, there was considerable increase in number of errors throughout the AOH period and, unlike the analogous parameters for the first group, they never did reach background levels to the end of the AOH period.

BP, HR and RR were recorded before, during and after the study in order to objectivize the mental stress caused by performance of tasks. The changes in these physiological parameters were insignificant in the first group of subjects. Thus, during work BP rose by a mean of 10/5 mm Hg, HR by 5-10/min and RR by 5-10 cycles/min.

Systolic and diastolic BP rose (by a mean of 15 and 10 mm Hg, respectively) in the absolute majority of subjects in the second group when performing their tasks. There were significant changes in external respiration. When they changed to the opposite mode of work it became irregular and increased by a mean of 20 cycles/min. HR increased by a mean of 20-30/min and, in some cases, reached 140-144/min.

These changes in physiological parameters of subjects in the second group were definitely closely related to the emotional and volitional sphere, as indicated by increased emotional excitability, motor and verbal disinhibition, irritability, marked reactions and poor performance of tasks.

Thus, the main difference between these groups was the type of adaptation of the body to altered living conditions (inert or plastic). These types of adaptation are manifested by typical dynamics of mental work capacity under conditions of simulated weightlessness using AOH. Individuals of the plastic

type, who had considerable psychophysiological reserves, adjusted faster and better to AOH conditions and, with the necessary training, are able to perform at a high level of mental work capacity during the period of acute physiological adaptation to weightlessness without excessive psychophysiological effort. The individual psychophysiological traits of subjects in this group, which enabled them to perform well under stress-producing conditions, are an occupational asset, since they enhance reliability of the human element in the "cosmonaut-spacecraft" system. These data are consistent with the findings of V. N. Myasishchev [17] and Ye. D. Khomskaya [26].

In individuals of the inert type, diminished productivity under AOH conditions, combined with significant changes in physiological parameters (HR, BP, RR), indicates that their psychophysiological reserves are either limited or largely depleted. Such individuals will probably be unreliable in difficult (including emergency) flight situations.

Our findings indicate that testing mental work capacity under AOH conditions constitutes a distinctive load test, which permits detection of discrete disturbances of mental work capacity that are not demonstrable under ordinary conditions.

There are grounds to believe that the obtained data can be recommended for use at the stages of screening and training spacecraft crews, in order to pick out individuals who are resistant and sensitive to weightlessness, in plotting cyclograms of cosmonaut performance, as well as in developing the set of psychoprophylactic and psychocorrective measures to maintain a high level of work capacity.

BIBLIOGRAPHY

1. Alyakrinskiy, B. S., KOSMICHESKAYA BIOL., No 1, 1980, pp 3-8.

2. Artishuk, V. N., Litsov, A. N., Stupnitskiy, V. P. et al., Ibid, No 5, 1974, pp 75-78.

3. Briedis, Yu. E., "Investigation of Human Work Capacity Under Severe Mental Stress and Some Means of Psychophysiological Optimization of Sensory and Mental Work," Riga, 1972.

4. Yegorov, A. S. and Zagryadskiy, V. P., "Psikhofiziologiya umstvennogo truda" [Psychophysiology of Mental Labor], Leningrad, 1973.

5. Yeremin, A. V., Bogdashevskiy, R. M. and Baburin, Ye. F., in "Nevesomost' (mediko-biologicheskiye issledovaniya)" [Weightlessness (Biomedical Investigations)], Moscow, 1974, pp 326-341.

6. Zav'yalov, Ye. S., Mel'nik, S. G., Chugunov, G. Ya. et al., KOSMICHESKAYA BIOL., No 1, 1970, pp 61-65.

7. Ioseliani, K. K., "Clinical and Psychological Tests in Expert Medical Certification of Pilots," author abstract of doctoral dissertation, Moscow, 1975.

8. Ioseliani, K. K. and Myasnikov, V. I., in "Problemy inzhenernoy psikhologii" [Problems of Engineering Psychology], Leningrad, 1979, pp 225-226.

9. Ioseliani, K. K. and Kiseleva, T. A., in "Metodiki issledovaniy v tselyakh vrachebno-letnoy ekspertizy" [Testing Methods in Expert Medical Certification of Pilots], Moscow, 1963, pp 214-223.

10. Kaznacheyev, V. P., "Sovremennyye aspekty adaptatsii" [Current Aspects of Adaptation], Novosibirsk, 1980.

11. Klauchek, S. V., "Dynamics of Human Work Capacity Parameters as Related to a Closed Environment," author abstract of candidatorial dissertation, Moscow, 1980.

12. Krupina, T. N. and Tizul, A. Ya., SOV. MED., No 7, 1978, pp 30-33.

13. Krylov, A. A., "Chelovek v avtomatizirovannykh sistemakh upravleniya" [Man in Automated Control Systems], Leningrad, 1972.

14. Leman, G., "Prakticheskaya fiziologiya truda" [Applied Industrial Physiology], Moscow, 1967, p 79.

15. Medvedev, V. I., in "Ergonomika. Printsipy i rekomendatsii" [Ergonomics--Guidelines and Recommendations], Moscow, Vyp 1, 1970, pp 127-160.

16. Mikhaylov, V. M., Alekseyeva, V. P., Kuz'min, M. P. et al., KOSMICHESKAYA BIOL., No 1, 1979, pp 23-28.

17. Myasishchev, V. N., "Kliniko-psikhologicheskiye issledovaniya lichnosti" [Clinical-Psychological Personality Tests], Leningrad, 1971, p 5.

18. Myasnikov, V. I., Novikov, M. A., Uskov, F. N. et al., in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii" [Adaptation to Muscular Activity and Hypokinesia], Novosibirsk, 1970, pp 127-128.

19. Narinskaya, A. L., in "Metodika issledovaniy v tselyakh vrachebno-letnoy ekspertizy," Moscow, 1963, pp 223-227.

20. Parin, V. V. and Krupina, T. N., in "Adaptatsiya k myshechnoy deyatel'nosti i gipokinezii," Novosibirsk, 1970, pp 134-135.

21. Pestov, I. D. and Geratevol', Z. Dzh., in "Osnovy kosmicheskoy biologii i meditsiny. T. 2. kn. 1. Ekologicheskiye i fiziologicheskiye osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine. Vol 2, Bk 1, Ecological and Physiological Bases of Space Biology and Medicine], Moscow, 1975, pp 324-369.

22. "Operator's Work Capacity (GOST 21033/75)," in "Ergonomika v opredeleniyakh. Metod. materialy" [Ergonomics in Definitions. Methodological Material], Moscow, 1980, p 76.

23. Sevast'yanov, V. I., in "Psikhologicheskiye problemy kosmicheskikh poletov" [Psychological Problems of Spaceflights], Moscow, 1979, pp 29-37.

24. Selye, H., "Essays on the Adaptation Syndrome," Moscow, 1960.

25. Ukhtomskiy, A. A., "Sobr. soch." [Collected Works], Vol 1, Leningrad, 1950.

26. Khomskaya, Ye. D., "Mozg i aktivatsiya" [The Brain and Activation], Moscow, 1972.

27. Khrunov, Ye. V., Khachatur'yants, L. S., Popov, V. A. et al., "Chelovek-operator v kosmicheskom polete" [Operators in Spaceflights], Moscow, 1974.

28. Chase, G. A., Grave, C. and Rowell, L. B., AEROSP. MED., Vol 37, 1966, pp 1232-1238.

29. Grether, V. F., ANN. N.Y. ACAD. SCI., Vol 134, 1965, pp 398-412.

30. Huddleston, H. F., SPACEFLIGHT, Vol 18, 1966, pp 268-274.

31. Lowrey, H. O. and Hoy, J. T., "Human Factors of the Lunar Logistics Mission," SAE PREPRINTS, No 302, 1961, p 111.

32. Ryback, R. S., Trimble, R. W., Lewis, O. F. et al., AEROSPACE MED., Vol 42, 1971, pp 408-414.

33. Simons, J. C. and Gardner, M. S., in "Proc. Inst. Environmen. Sci. Nat. Meet.," Washington, 1961, pp 371-378.

34. Summers, Leland, G., in "Physiological and Performance Determinants in Manned Space Systems," Baltimore, 1965, pp 149-165.

35. White, S. C., Berry, C. A. and Hessberg, R. R., "Effects of Weightlessness on Astronaut: a Summary," Berlin, 1972.

UDC: 612.886.1.014.45.014.47:531.15

EFFECT OF ROTATION AND VIBRATION ON HUMAN ORIENTATION RELATIVE TO GRAVITY VERTICAL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 14 Nov 83) pp 24-28

[Article by O. A. Vorob'yev and V. V. Ivanov]

[English abstract from source] The man's ability to get oriented in relation to the gravitational vector was investigated. The test subjects were exposed either to rotation in 1 m arm centrifuge or tilting in a chair. They were simultaneously exposed to total-body vertical vibration of 20 Hz. As the exposure continued, the ratio of the perceived vertical (in the absence of visual keys) and the apparent body position changed significantly. It is concluded that the tests used to evaluate the pilot ability for spatial orientation should include evaluations of the subjective vertical and body position relative to the gravitational vector. The tests should be performed during exposures to simulated dynamic flight factors.

[Text] One of the important elements of a pilot's spatial orientation is precise localization of his body and objects in the cabin of an aircraft in relation to "top-bottom" coordinates during exposure to the dynamic factors of flight. For this reason, investigation of the ability to determine the direction of the gravity vertical has been suggested as a test to assess reliability of pilots in case of impaired inflight spatial orientation [15].

It is known that when there is a change in the position of the body in relation to the gravity vector, as well as under the effect of lateral acceleration during rotation on a centrifuge, there is change in accuracy of the subject's definition of the vertical. However, the relevant psychophysiological mechanisms of this phenomenon have not yet been determined [3]. In the vast majority of works published previously [1, 2, 4 and others], studies were pursued mainly of the dynamics of the visually perceived vertical. Moreover, as we have noted, in order to assess man's susceptibility to impaired spatial orientation it is necessary to determine accuracy of orientation of the body in relation to the gravity vector [12], in addition to determination of the vertical. Considering the foregoing, it was deemed important to investigate the adequacy and informativeness of different tests to determine the capacity for spatial

orientation in order to use the findings in screening and special training of flight personnel.

Our objective here was to investigate man's ability to determine the direction of the vertical and position of his body during exposure of the otolith system to accelerations, as well as under the influence of total-body vertical vibration.

Methods

We determined the capacity for orientation relative to the gravity vector (true vertical) by means of a special instrument, in which the subject set a rod, which rotated freely in the frontal plane (banking plane), in the position of the so-called subjective haptic vertical (corresponding to the vertical perceived by sense organs) or parallel to the body's midline in relation to the gravity vector. The rod could not be moved in other planes and such moves were not recorded. The angle of deflection of the rod (lever) away from the direction of the true vertical was measured with potentiometric sensors and recorded on an automatic ink-recorder. The instrument was calibrated in such a way that one could calculate the deflections of the lever from the true vertical in the banking plane in degrees. In all instances, the subjects handled the lever with their right hand, sitting erect with the eyes closed. In the intervals between manipulations, the subject lowered the lever to one of its extreme positions.

Two series of tests were conducted. In the first one, we simulated production of the illusion of banking by rotation subjects on a small CF-10 vestibulometric centrifuge (Figure 1a). The subjects were seated, facing the direction of movement of the stand, in a semihard chair (the seat was padded with porolon 15 mm in thickness) 1 m away from the axis of rotation. At first we recorded background data: in all cases in this series of tests, determination of both the subjective vertical and body position was repeated 4 times in succession: the first time, from the extreme right position of the lever, the second time, from the extreme left, etc. Then the subjects were rotated in a clockwise direction (to the left) about the vertical axis at an angular velocity of 110°/s, so that the resultant force of gravity and centrifugal force would constitute an angle of about 20° with the direction of the true vertical. Each subject was rotated twice, in one case he set the lever only in the position of the subjective vertical throughout the test period and in the other (the order was randomized), parallel to the midline axis of the body; there were 30-45-min intervals between the two rotations. Each exposure to rotation lasted 15 min, during which the subject periodically (when so ordered by the physician) manipulated the lever, starting at the time of reaching a constant rate of rotation. After the chair was stopped, both tested parameters were recorded. A total of 17 healthy men 23-48 years old participated in these studies.

In the second series of tests, the sensation of banking was produced by tilting the seat successively 5 and 10° to the right during exposure of the entire body to vibration. For this purpose, a special device was installed on a VEDS-1500 vibration stand, on which there was a hard seat for the subject (Figure 1b). There was a lever in front of the subject, which he first moved twice from the extreme positions into the subjective vertical position at

each angle of tilt of the goniometer stand and then with its help tracked down the position of his body. These parameters were recorded before, during and after exposure at 15-min intervals. We used vertical vibration (frequency 20 Hz) and vibrational acceleration (7 m/s^2) which occurs in helicopters [13]. Six healthy men participated in these studies. We ran six control tests and six tests with vibration on each of them.

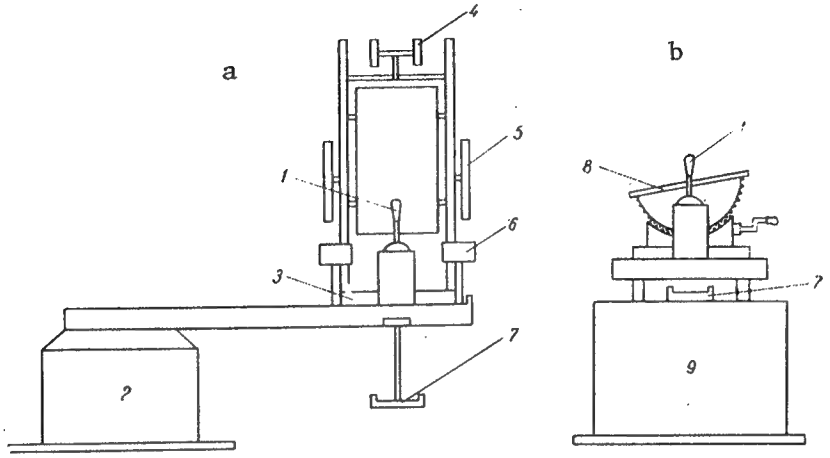


Figure 1. Diagram of equipment used in the study

a) small CF-10 vestibulometric centrifuge
b) vibration stand equipped with goniometer
1) lever (rod) of instrument to determine capacity for spatial orientation
2) centrifuge base
3) chair seat
4) headrests
5) body rests on chair
6) elbow pads
7) foot support
8) tilting goniometer platform
9) vibration stand base

Results and Discussion

When turning on the centrifuge, all of the subjects developed (to varying degrees) the illusion of a left bank, manifested by the sensation that their body was tilting with the chair. The severity of these sensations, according to the verbal reports of the subjects, gradually diminished as rotation time increased. The obtained mean data on dynamics of direction of subjective vertical and perceived position of the body's midline (PPBM) are illustrated in Figure 2.

Figure 2 shows that in the 1st min of rotation there is equivalent degree but opposite deviation from the vector of gravity of both the subjective vertical and PPBM. Then, starting in the 5th min of rotation, the angle of deviation of the subjective vertical has a tendency toward increasing, which is also

typical of the dynamics of the visual vertical [5, 8]. However, it should be mentioned that the deviations of the subjective vertical found in our studies were considerably smaller than the angle between the direction of the gravity-inertial resultant and gravity vector, which determines the severity of the oculogravic illusion that arises under the influence of inertial forces on the otolith system.

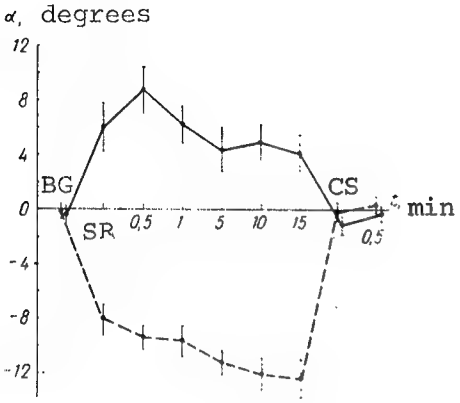


Figure 2.
Dynamics of position of subjective vertical and PPBM with development of banking illusion on small CF-10 centrifuge
X-axis, time of examination; y-axis, angle of deviation from gravity vector. Solid line, deviation of PPBM, dash line, position of subjective vertical
BG) background
SR) start of rotation
CS) after centrifuge is stopped
+) deviation to left of axis of rotation
-) deviation to the right of angle of rotation

In addition, as rotation time increased there was some decrease in angle of PPBM deviation and, starting in the 5th min it was 1/2 to 2/5 the deviation of the subjective vertical. In other words, at the start of exposure to centrifugal force the severity of the banking illusion is characterized to equal extent by the angle of deviation of both the subjective vertical and PPBM, whereas at the later stages this illusion is reflected primarily by the deviation of the subjective vertical in relation to the gravity vector.

Analysis of the individual results also revealed that in some subjects this tendency of correlation between subjective vertical and PPBM was quite marked, whereas in others there were no appreciable changes throughout the period of rotation of angles of these parameters (see Table).

Such dynamics of correlation between the subjective vertical and PPBM when simulating the illusion of banking on the small centrifuge were apparently attributable to the distinctions of interaction between otolith receptors and mechanoreceptors of the human body during perception of the gravity vertical in the absence of visual information. Thus, the decrease in angle of deviation of PPBM with increase in rotation time could be attributed to the influence of the adaptation process, which develops rapidly in muscular and articular receptors when the body is in a fixed position [9], as was the case in our studies. The coefficients of correlation between the magnitude of change in severity of the banking illusion characterized verbally by the subjects and angle of deviation of PPBM in the course of the study constituted 0.86. Consequently, our findings indicate that the discussed method of orientation in relation to the gravity vector makes it possible to assess rather fully the extent of banking illusions in the event that an overall characteristic of the spatial position of both the subjective vertical and PPBM is used.

The results of the tests on the vibrating stand (Figure 3) revealed that, with exposure to vibration, the accuracy of determining the subjective vertical

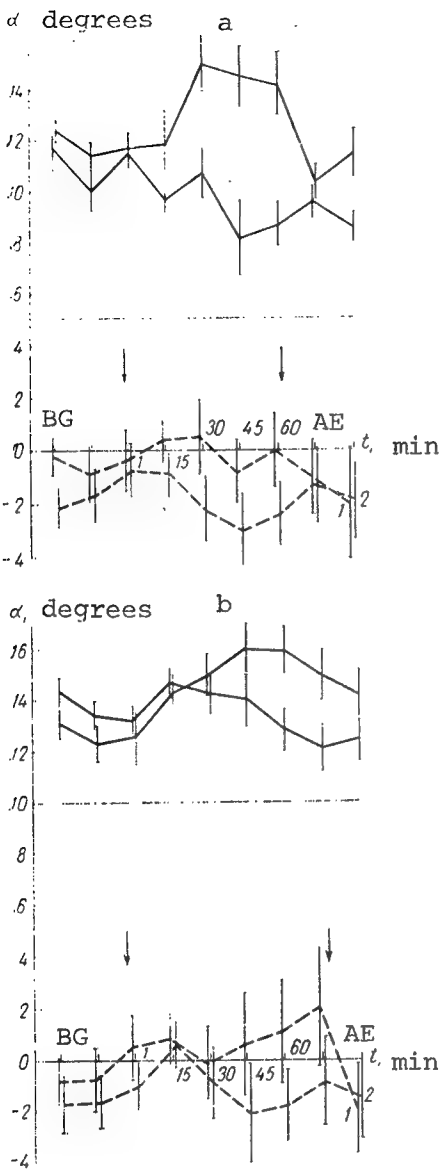


Figure 3.
Dynamics of parameters of orientation relative to gravity vertical during exposure to vibration
X-axis, time of test; y-axis, angle of deflection from gravity vertical. Arrowheads show start and end of vibration
a) goniometer angle (shown by interrupted line with dots) of 5°
b) goniometer angle of 10°
1) vibration
2) control
+) deviation to the right
-) deviation to left of gravity vector
BG) background
AE) aftereffect
Solid line, PPBM; dash line, position of subjective vertical

did not differ appreciably from control data. At the same time, the degree of deviation of PPBM as vibration exposure time increased underwent statistically significant changes, as compared to values obtained without vibration, and this was particularly evident at a 5° angle of deflection of the goniometer platform. Thus, starting with the 30th min and to the end of vibration exposure, we observed significant overestimation of the angle of deviation of the PPBM. Perhaps this was due to the marked activating effect of vibration at this frequency on reactions of the myoneural system [7]. In the aftereffect period the accuracy of estimating PPBM returned. Consequently, as shown by the obtained data, it is necessary to use vibration factors for adequate simulation of banking illusions as related to helicopters. In addition, during ground-based simulator training of helicopter pilots it is desirable to take into consideration the modulating effect of the vibration factor on accuracy of determining the body's spatial position in relation to the gravity vector.

Analysis of Figure 3 revealed that, in the control studies (without vibration) with the goniometer at a 5° angle the subjects attributed their spatial position to deflection of both the PPBM and subjective vertical in relation to the normal to the goniometer platform. Conversely, at an angle of 10° there was more marked deviation of the subjective vertical, exceeding by 2.5-3.0 times the deviation of PPBM. The findings indicate that, when on a tilted goniometer platform, the nature of orientation in relation to the seat surface is analogous to orientation when rotating on the centrifuge: the correlation between angles of deflection of the subjective vertical and PPBM at an initial angle of 5° is equivalent to the one in the 1st min of rotation, and at an angle of 10°, to the subsequent period of rotation. We

were impressed by the fact that the angles of deviation (relative to the gravity vector) of both the subjective vertical and PPBM did not differ significantly at 5 and 10° tilt angles of the goniometer platform. These findings are consistent with previously obtained data concerning the visual vertical, which indicated that it shifts in the direction of inclination after a period of preliminary inclination. This is interpreted as an aftereffect of adaptation of the proprioceptive system [14]. In addition, compensatory voluntary motor reactions of the subject on the goniometer could have played some part also, in view of the absence of lateral restrictions on the seat, whereas in the centrifuge seat the subject's body and head were immobilized. It is known that muscular contractions during active movements generate reafferentation [10], which enables man to be more accurately oriented in relation to the gravity vector. It must also be noted that when the goniometer is tilted, the foot support remained in horizontal position at all times, and this probably had an additional effect on articular mechanoreceptors involved in perception of body inclinations away from the vertical position [11].

Examples of accuracy of orientation in an altered gravity-inertial field (angle of deviation from gravity vector, in degrees)

Subject	Parameter	Stage of study							
		BG	SR	inclination angle, degrees					SC
				0.5	1	5	10	15	
B-a	Subjective vertical	+0,1	—9,8	—13,6	—16,3	—16,0	—17,3	—19,5	—1,6
	Angle of body tilt	+0,5	+15,8	+13,6	+7,3	—2,1	—1,1	+4,0	+0,8
Zh-v	Subjective vertical	—0,3	—4,0	—2,5	—0,4	—6,4	—3,0	—5,4	—1,8
	Angle of body tilt	—2,3	+6,4	+12,8	+10,6	+9,8	+13,6	+15,0	+0,3

Key: BG) background SR) start of rotation SC) centrifuge stopped

Analysis of individual results revealed that, while the subjects determined PPBM more accurately than the subjective vertical in the goniometer test, when rotated on the centrifuge they presented a deviation primarily of the subjective vertical. Conversely, while mostly PPBM errors were recorded in the former case, there was less deviation of the subjective vertical in the latter. On the basis of these data it can be assumed that the correlation between dynamics of the subjective vertical and PPBM typical of a specific individual, which is manifested by different conditions of developing the sensation of banking, reflects interaction between vestibular and proprioceptive modalities in perception of spatial coordinates, with consideration of individual distinctions of adaptation and other characteristics of these sensory systems.

However, neither the method of Witkin to determine the capacity for spatial orientation nor its modification take into consideration the modulating effect of adaptation processes in the vestibular-proprioceptive complex to such a characteristic of man's mode of orientation as egocentricity, i.e., independently of location of visually perceived cues [12]. At the same time, it has been established that a pilot's use of the egocentric system of coordinates

lowers the efficiency and reliability of assessing the spatial position of an aircraft [6]. In this regard, it can be assumed on the basis of the foregoing that development of methods of assessing the individual profile of vestibular-proprioceptive orientation in an altered gravity-inertial field could be one of the means of improving tests to assess a pilot's capacity for spatial orientation. Our findings warrant the conclusion that, in developing such a method, it is desirable to make a combined determination of the dynamics of subjective vertical and body position during simulation of the effects on man of dynamic factors of flight in aircraft.

BIBLIOGRAPHY

1. Bokhov, B. B. and Kantor, S. L., FIZIOLOGIYA CHELOVEKA, Vol 3, No 2, 1977, pp 308-316.
2. Bokhov, B. B. and Taranenko, Yu. N., KOSMICHESKAYA BIOL., No 4, 1979, pp 80-83.
3. Vyurpillo, E., in "Eksperimental'naya psikhologiya" [Experimental Psychology], Moscow, Vyp 6, 1978, pp 199-236.
4. Kurashvili, A. Ye. and Babiyak, V. I., KOSMICHESKAYA BIOL., No 2, 1974, pp 42-50.
5. Idem, "Fiziologicheskiye funktsii vestibulyarnoy sistemy" [Physiological Functions of the Vestibular System], Leningrad, 1975.
6. Lapa, V. V. and Lemeshchenko, N. A., KOSMICHESKAYA BIOL., No 1, 1982, pp 45-49.
7. Nikandrov, A. V. and Kopysov, V. S., "Vibratsionnyy massazh v podgotovke tyazheloatletov" [Vibrating Massage in Training Weightlifters and Wrestlers], Moscow, 1981.
8. Graybiel, A. and Clark, B., quoted by R. A. Peters: "Dynamics of the Vestibular System and Their Relation to Motion Perception, Spatial Disorientation, and Illusions," Washington, 1969, p 186.
9. Day, R. H. and Wade, N. J., PSYCHOL. BULL., Vol 71, 1969, pp 33-42.
10. Von Holst, E. and Mittelstaedt, H., NATURWISSENSCHAFTEN, Vol 37, 1950, pp 464-476.
11. Lackner, J. R. and Graybiel, A., EXP. BRAIN RES., Vol 44, 1981, pp 312-316.
12. Lager, C., in "Pilot Reliability," Stockholm, 1974, pp 150-154.
13. Thorne, R. G., AERONAUT. J., Apr 1974, pp 167-180.
14. Wade, N. J., BRIT. J. PSYCHOL., Vol 64, 1973, pp 351-361.
15. Witkin, H. A., PSYCHOL. MONOGR., Vol 63, 1949, pp 1-46.

UDC: 612.766.1/.2-08:612.117.2

RHEOLOGICAL PARAMETERS OF BLOOD AT DIFFERENT LEVELS OF MOTOR ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 24 Aug 83) pp 29-31

[Article by A. P. Ivanov, I. B. Goncharov and A. F. Davydkin]

[English abstract from source] Blood rheological parameters of essentially healthy people were examined during exercises of a maximal workload and 14-day head-down tilt. The results obtained indicate that in people performing normal and increased motor activity some rheological parameters were different. Changes in the rheological parameters of blood after head-down tilt and exercises with a maximal workload suggest the existence of a blood viscosity threshold above which physical work capacity declines significantly. The capacity can be restored through a correction of blood viscosity in the recovery period. The basic rheological properties of blood can be improved by regular physical training.

[Text] It is a known fact that man's physical work capacity depends largely on the body's oxygen-transport capabilities (OTC). Minute volume (MV) is an important factor that determines these capabilities. This parameter depends to some extent on blood rheological properties, which are determined primarily by its viscosity. Thus, increased blood viscosity increases peripheral vascular resistance to blood flow, which hampers venous return of blood to the heart and, consequently, could lower MV [11], and this means it could also lower OTC.

The results of studies conducted by a number of authors [9, 14, 15, 16] have shown that physical exercise, particularly at submaximum and maximum aerobic intensity, is associated with exit of fluid from the vascular bed without an associated quantitative change in erythrocyte mass [2, 9]. Analogous data were obtained in experiments with simulation of weightlessness [6]. Loss of fluid from the vascular bed must, of course, lead to increase in blood concentration and, consequently, in blood viscosity.

In view of the foregoing, it is of theoretical and practical interest to investigate the rheological parameters of blood in essentially healthy individuals submitted to different extreme conditions (physical exercise at the level of maximum oxygen uptake--MOU, and antiorthostatic hypokinesia--AOH [head-down tilt]), differing in levels of physical conditioning.

Methods

We had 3 groups of essentially healthy men, 22-35 years of age, under observation. The 1st and 2d groups consisted of 18 men each whose motor activity was ordinary and the 3d, 18 athletes who were in training for endurance: 11 medium and long distance runners, 3 bicyclists and 4 oarsmen. Five of the athletes were ranked in the 1st category, 5 were candidates for sports masters, 7 were masters of sports and 1 was a sports master of the international class. The subjects of the 1st group spent 14 days on strict bedrest in anti-orthostatic position (head-down tilt at -8°); the 2d and 3d groups exercised with progressive increase in load on a Monark bicycle ergometer. At first their load was 500-600 kg-m/min for 5 min, then after 3 min, 1300-1750 kg-m/min also for 5 min. These two loads were used to determine the size of the third (basic) load. The third load began after resting for 5 min and lasted as long as the subjects could perform. This load was selected so as to require performance at MOU level. Pedaling rate of 60 r/min paced with a metronome was maintained constantly with all load levels. Blood was drawn from the ulnar vein before and after exercise to assay hematocrit (Hct), hemoglobin concentration (Hb) and blood viscosity. In addition, we determined the parameters of caisson viscosity (K), limit of blood viscosity (τ_0) and we calculated the coefficient of red cell aggregation (A). Blood viscosity at 3 velocities of "shift" (0.5, 1.0 and 5.0 s^{-1}) was determined with the rotating viscometer of V. N. Zakharchenko at a temperature of 25±0.1°C. Loss of plasma (Δ% pV) from the vascular bed was calculated using the method proposed by Dill and Costill [10].

Results and Discussion

Table 1 lists base parameters of blood for all three groups of subjects.

The results are indicative of differences in several of the base parameters of blood in the 3d group of subjects, as compared to representatives of the 1st and 2d groups.

Table 1. Mean base rheological parameters of blood (M±m)

Group of subj.	Viscosity (cpoise) at shift velocity of			K, cpoise	τ_0, dynes/cm^2	A, dynes/cm^2×10^{-6}	Hct, %	Hb, g%
	0.5 s^{-1}	1.0 s^{-1}	5.0 s^{-1}					
1	25,81 ±1,05**	18,29 ±0,70**	10,37 ±0,48	5,33 ±0,39	0,0376 ±0,0060*	0,595 ±0,057	47,20 ±0,66*	15,70 ±0,55
2	24,45 ±1,76*	17,66 ±0,97*	10,19 ±0,74	5,76 ±0,46	0,0378 ±0,0056*	0,639 ±0,105	47,83 ±0,51**	15,45 ±0,20
3	19,66 ±1,06	14,67 ±0,63	9,40 ±0,51	5,97 ±0,57	0,0229 ±0,0039	0,490 ±0,097	45,39 ±0,50	15,12 ±0,28

*Differs reliably from 3d group parameters according to Student's t criterion at $P<0.05$.
**Same at $P<0.01$.

An increase in blood flow rate is one of the adaptive mechanisms aimed at adequate delivery of oxygen to functional muscles during exercise. In turn,

an increase in blood velocity also implies an increase in velocity of shift in the flow of blood, and the lower the base rheological parameters of blood, the higher the velocity of shift. It is important to note that, under conditions of shifting flow, oxygenation of blood is directly related to velocity of shift in the range of velocities of shift from 0 to 230 s^{-1}. It becomes obvious that the lower the base viscosity of blood, limit of blood viscosity and hematocrit in representatives of the 3d group potentially increase OTC and, consequently, human endurance of exercise.

Table 2 lists the mean rheological parameters for subjects in the three groups studied after the load (maximum exercise at MOU level and 14-day AOH -8°).

Table 2. Mean rheological parameters after test factors (M±m)

Group of subj.	Viscosity (cpoise) at shift velocity			K, cpoise	τ_0, dynes/cm^2	A, dynes/cm^2×10^{-6}	Hct, %	Hb, g%	Δ% pV
	0,5 $^{-1}$	1,0 $^{-1}$	5,0 $^{-1}$						
1	33,34	24,75	15,08	9,07	0,0397	0,513	50,66	17,73	—10,1
	±2,18	±1,55	±1,06	±0,80	±0,0040	±0,069	±1,23	±0,47	±4,37
2	36,64	26,08	14,98	7,84	0,0592	0,628	52,11	16,79	—15,9
	±1,60	±0,84	±0,72	±0,60	±0,0105	±0,103	±0,46	±0,26	±1,27
3	33,55	23,87	14,20	7,44	0,0570	0,730	50,00	16,30	—14,9
	±1,26	±0,92	±0,54	±1,38	±0,0090	±0,120	±0,71	±0,71	±1,48

The data listed in Table 2 indicate that there was significant change in all of the rheological parameters studied in all groups of subjects, as compared to their base values. Since both exercise and AOH are associated with exit of plasma from the blood stream without concomitant quantitative change in erythrocyte mass, the main factor causing worsening of blood rheological parameters in the three tested groups after use of these factors is the increase in blood concentration. This is confirmed by the significant increase in concentration of hemoglobin and hematocrit, as compared to the base level (see Tables 1 and 2).

With increase in concentration of hemoglobin in blood, there is increase in its oxygen capacity and, consequently, potential increase in the body's OTC. At a certain stage this fact could be viewed as one of the mechanisms of human adaptation to large physical loads. On the other hand, this is associated with increase in blood viscosity, which has an adverse effect on cardiac output [11].

The reliable decrease in oxygen uptake and decrease in CO_2 output in people on strict bedrest or submitted to AOH, which have been observed by several authors [3, 4, 8], are apparently related to increase in blood viscosity. The latter leads to increase in general peripheral resistance to blood flow and thus could lower MV [11].

The absence of appreciable differences in the end results is, in our opinion, a rather important factor, particularly if we consider that the subjects in

the second and third groups refused to continue with the test at very similar levels of rheological parameters. The force of the exercise done on the ergometer by the third group of subjects was considerably greater than that done by the second group. This indicates that there is a limit of blood concentration, beyond which it is virtually impossible to perform physical work that requires specific effort. If we assume that such a limit does indeed exist, it is hard to expect retention of high physical work capacity (endurance) in subjects of the first group submitted to AOH. Indeed, a decrease in work capacity of subjects submitted to factors simulating weightlessness had been demonstrated by many researchers and is not questioned [5, 13]. Probably, the increase in blood viscosity and, consequently, impairment of the body's OTC play a deciding role in lowering physical work capacity. In this case, it can be assumed that the decrease demonstrated by several authors [1, 7, 12] in cellular elements of blood against the background of fluid loss from the vascular bed in individuals during actual spaceflights is one of the adaptive mechanisms aimed at lowering blood viscosity and related disturbances of OTC. It is imperative to serach for methods of correcting blood viscosity in the recovery period following the extreme states studied in order to restore physical work capacity.

BIBLIOGRAPHY

1. Vorob'yev, Ye. I., Gazenko, O. I. and Gurovskiy, N. N., KOSMICHESKAYA BIOL., No 5, 1976, pp 3-18.

2. Gandel'man, A. B., Rappoport, A. B., Yevdokimova, T. A. et al., FIZIOLOGIYA CHELOVEKA, Vol 3, No 2, 1977, pp 355-361.

3. Katkovskiy, B. S., KOSMICHESKAYA BIOL., No 5, 1967, pp 67-71.

4. Kovalenko, Ye. A. and Gurovskiy, N. N., "Gipokineziya" [Hypokinesia], Moscow, 1980, pp 55-62.

5. Idem, Ibid, pp 85-94.

6. Kozinets, G. I., Belakovskiy, M. S., Ushakov, A. S. et al., KOSMICHESKAYA BIOL., No 3, 1983, pp 48-51.

7. Legen'kov, V. I., Balakhovskiy, I. S., Beregovkin, A. V. et al., Ibid, No 1, 1973, pp 39-45.

8. Mikhasev, M. I., Sokolov, V. I. and Tikhonov, M. A., in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 13, 1969, pp 71-78.

9. Van Beaumont, W., Strand, J. C., Petrovsky, J. S. et al., J. APPL. PHYSIOL. PHYSIOL., Vol 34, 1973, pp 102-106.

10. Dill, D. B. and Costill, D. L., Ibid, Vol 37, 1974, pp 244-248.

11. Ekblom, B. and Hermansen, L., Ibid, Vol 25, 1968, pp 619-625.

12. Fisher, C. L., Johnson, P. S. and Berry, C. A., J.A.M.A., Vol 200, 1967, pp 199-203.

13. Graveline, D. E., Balke, B., McKenzie, R. E. et al., AEROSPACE MED., Vol 32, 1961, pp 387-400.

14. Gregersen, M. L., Dill, D. B. and Meade, J., in "Medical Physiology," ed. P. Bard, St. Louis, 1956, p 758.

15. Joye, H. and Poortmans, J. R., MED. SCI. SPORTS, Vol 2, 1970, pp 187-190.

16. Poortmans, J. R., J. APPL. PHYSIOL., Vol 30, 1970, pp 190-192.

UDC: 612.13+612.17].014.47:612.76

COMPARATIVE CHARACTERISTICS OF CENTRAL HEMODYNAMICS AND CIRCULATORY REDISTRIBUTION REACTIONS TO ACTIVE AND PASSIVE ORTHOSTATIC TESTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 25 Jul 83) pp 31-39

[Article by G. S. Belkaniya and V. A. Dartsmeliya]

[English abstract from source] Typological characteristics of central and peripheral (legs and viscera) circulation were identified in 90 clinically healthy people exposed to active and passive orthostatic tests. The following three hemodynamic states were distinguished: hypokinetic, hyperkinetic and intermediate types of circulation. As compared to the passive tests, in the active states cardiac output decreased, leg blood flow increased and viscera blood flow decreased. At the stage of stabilized hemodynamics inotropic cardiac stimulation was predominant during passive orthostatic tests. In the former tests changes in cardiac output and blood redistribution between leg and viscera circulations were more distinct. Mechanisms of hemodynamic changes are discussed.

[Text] Active and passive orthostatic tests have been used for a long time in clinical and experimental practice to assess the functional state of the cardiovascular system and neurohumoral mechanisms of regulation of circulation. However, there is only fragmentary information in the literature concerning the comparative characteristics of hemodynamic changes during active and passive orthostatic tests [12-14].

The results of recent studies [1, 2, 5, 7] indicate that redistribution changes in central and peripheral hemodynamics are very important to compensation of the hydrostatic factor when the body is in orthostatic position. The differences between active and passive orthostatic positions also determine differences in degree of strain on regulatory mechanisms of circulation [1, 2]. Studies in this direction are important, not only to confirm the conception of relevance of hydrostatic and functional redistribution of blood flow to control of circulation in orthostatic position, but also to expand the capabilities of physiological interpretation of results obtained and increase the diagnostic informativeness of orthostatic tests.

Our objective here was to make a comparative study of external respiration, central and peripheral hemodynamics in healthy subjects during active and passive orthostatic tests.

Methods

Using a standardized method [3, 4], we performed active and passive orthostatic tests on 90 clinically healthy subjects 24 to 45 years of age, on different days after a 5-7-day stay at a hospital.

Spirography was used to assess the basic parameters of external respiration. Central hemodynamics were studied by tetrapolar thoracic rheography [8]. On the basis of the latter, in order to assess peripheral hemodynamics and redistribution of circulation we used the technique of regional tetrapolar rheography which we modified somewhat [6, 8, 11] and which enabled us to assess blood flow dynamics in the viscera and muscles of the pelvic girdle and extremities. The desirability of testing these parts of the body is validated because of the most marked redistribution in orthostatic position of blood flow between the vascular pools of internal organs and skeletal muscles involved in active standing [1].

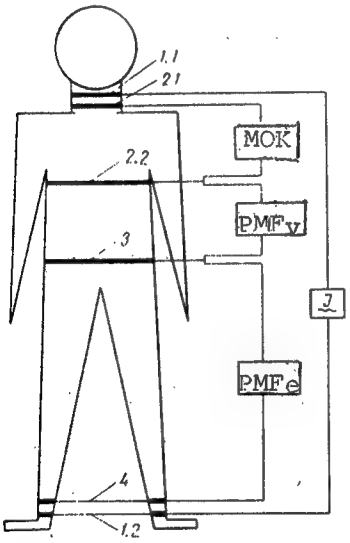


Figure 1.
Diagram of placement of electrodes for rheographic examination of central and peripheral hemodynamics. Explanation given in the text
МОК) circulation volume or cardiac output

Figure 1 illustrates how electrodes are placed and connected to record parameters of central and regional hemodynamics. The generator (current) electrodes of an RPG2-02 rheoplethysmograph were placed as follows: first circular electrode on the neck (see Figure 1, 1.1), the second, paired, in the lower third of the leg above the malleoli (1.2). Potential (measuring) electrodes were placed by the standard method [8]: one on the neck (2.1) and the other on the trunk on the level of the xiphoid process (2.2).

Measurement of general blood flow in internal organs was made between the potential electrode on the lower abdomen, below the umbilicus (*3*) and electrode on the trunk (2.2). Blood flow in pelvic girdle muscles and muscles of the limbs was measured between electrode *4* and the pair of electrodes placed above the malleoli (*4*). The distance between the current and closest potential electrodes was at least 3-4 cm.

Stroke volume (SV) was calculated using the standard formula [8]:

$$SV = 150 \frac{L^2}{Z^2} \cdot A_{dif} \cdot Tu, \text{ ml}$$

The parameters of minute blood flow in viscera (PMFv) and extremities (PMFe) were determined from the following general condition:

$$PMF = \frac{L^2}{Z^2} \cdot A_{dif} \cdot T_u \cdot HR, \text{ arbitrary units}$$

where L, Z, A_{dif} and T_u correspond to the rheographic characteristics of the measured part of the body and HR is heart rate.

For analysis we used indexed (scaled to body surface) parameters of central hemodynamics: stroke index (SI, in $m\ell/m^2$), cardiac index (CI, ℓ/m^2), specific peripheral resistance of vessels (SPR, dyne•s•cm^{-5}). Cardiac contractility was assessed by the amplitude of the differential rheogram (A_{dif}) which reflects the rate of ejection of blood at the first phase of the ejection period [10].

Regional hemodynamics were assessed by the PMFv and PMFe and according to nominal parameters of regional vascular resistance in internal organs (PRRv = BPm/PMFv•100, arbitrary units) and extremities (PRRe = BPm/PMFv•100, arbitrary units), where BPm is mean arterial pressure.

We used the Korotkov method to measure systolid (BPs) and diastolic (BPd) arterial pressure (mm Hg). BPm was calculated with the formula, BPm = BPd + 0.42 (BPs - BPd).

External respiratory function was evaluated by minute oxygen uptake scaled to body surface (O_2U, $m\ell/m^2$), respiration rate (RR/min), tidal volume (TV, $m\ell$) and minute volume (MV, $m\ell$/min). We calculated complex cardiorespiratory parameters: oxygen pulse (OP - O_2U/HR) and parameter of arteriovenous difference (AVD = O_2U/CI).

These parameters were recorded under basal metabolic conditions in a clinostatic position. For the next 20 min of orthostatic testing, the parameters were recorded in the 1st, 5th, 10th, 15th and 20th min. The hemodynamic changes were assessed as percentage of parameters in clinostatic state taken as 100%.

Results and Discussion

Analysis of typological distinctions of central circulation enabled us to distinguish three hemodynamic states in healthy subjects during orthostatic testing. The parameters considered were analyzed according to the transitional period (1-5 min) and period of stabilized hemodynamics (10-20 min) of orthostatic state. We made a distinction between hypokinetic (I), hyperkinetic (III), as well as intermediate or mixed (II) types according to changes in cardiac output during the period of stabilized hemodynamics. These types are characterized by individual features of hemodynamic state in orthostatic position, and for this reason they were reproducible upon repeated checking and persisted during the passive orthostatic test. The comparative data illustrated in Figure 2 demonstrate distinct differences between the circulation types in orthostatic position with regard to the basic hemodynamic parameters. There were particularly distinct differences in dynamics of SI, CI, SPR and A_{dif}, which are parameters reflecting the state of the basic hemodynamic mechanisms of maintaining BPm.

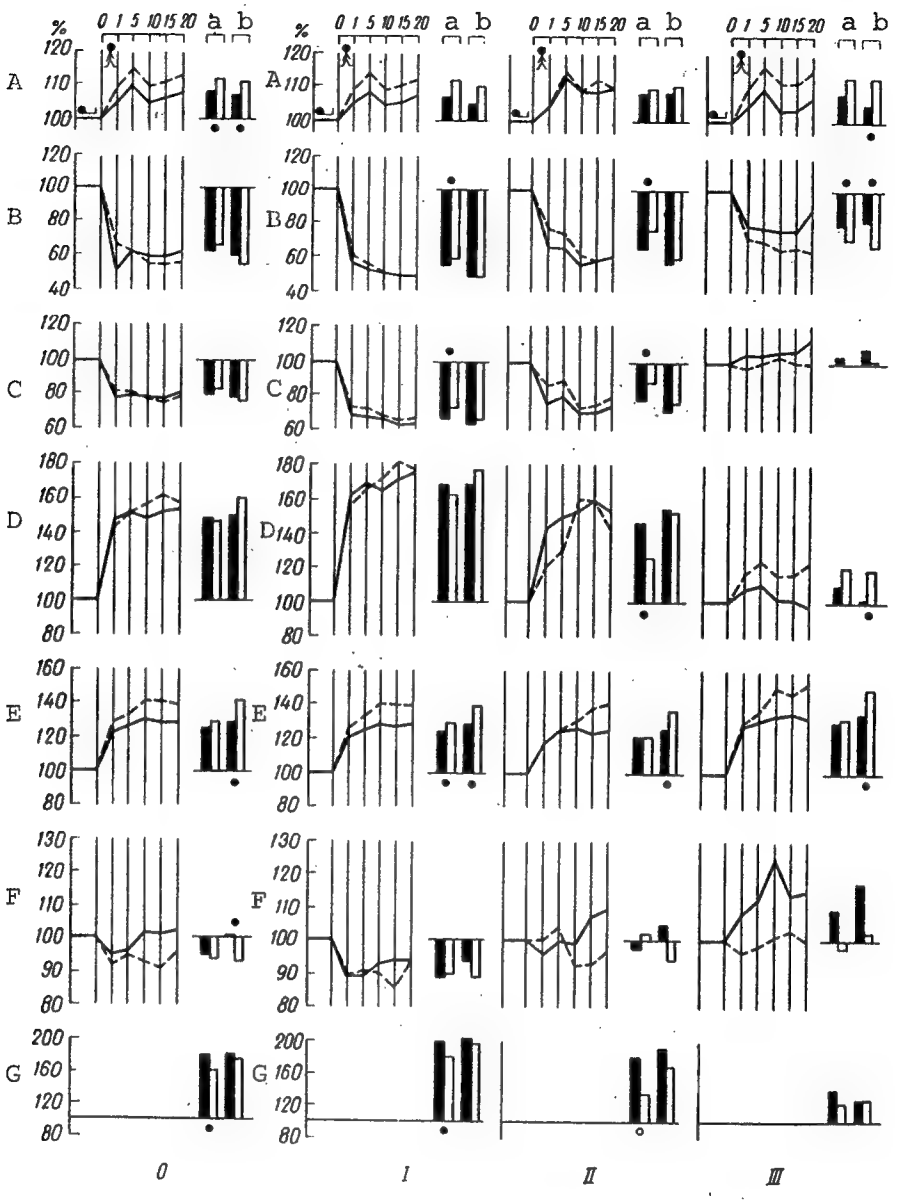


Figure 2. Dynamics of parameters of central hemodynamics in healthy subjects during active (solid lines) and passive (dash lines) orthostatic tests

Here and in Figures 3 and 4, x-axis: 0--characteristics of total sample, I, II and III--types of hemodynamic states in orthostatic position; y-axis, time (min).

The bars show parameters of transitional period (a) and stabilized state (b) during active (black bars) and passive (white) orthostatic tests. The dots indicate reliable differences ($P<0.05$). A-G refer to BPm, SI, CI, SPR, Adif and parameter of arteriovenous difference for O_2, respectively.

All three types (I, II and III) differ reliably from one another in the passive orthostatic test (I and II--$P<0.05$; II and III--$P<0.001$) in changes of visceral blood flow (according to PMFv). We should call attention to the fact that the

hemodynamic states during orthostatic tests differ from one another, not only in quantitative characteristics but also in qualitative manifestations of changes in regional blood flow, which is particularly important (Figure 3). Thus, while marked and reliable decline of PMF in viscera (by 26%, $P<0.01$) is observed with the hypokinetic type, in hyperkinetic state there is the opposite reaction--blood flow increases by 18% ($P<0.01$) and 23% ($P<0.01$) in the transitional period and period of stabilized central hemodynamics, respectively. With type II, the changes in PMFv are intermediate, being similar in direction to the characteristics of type I (hypokinetic).

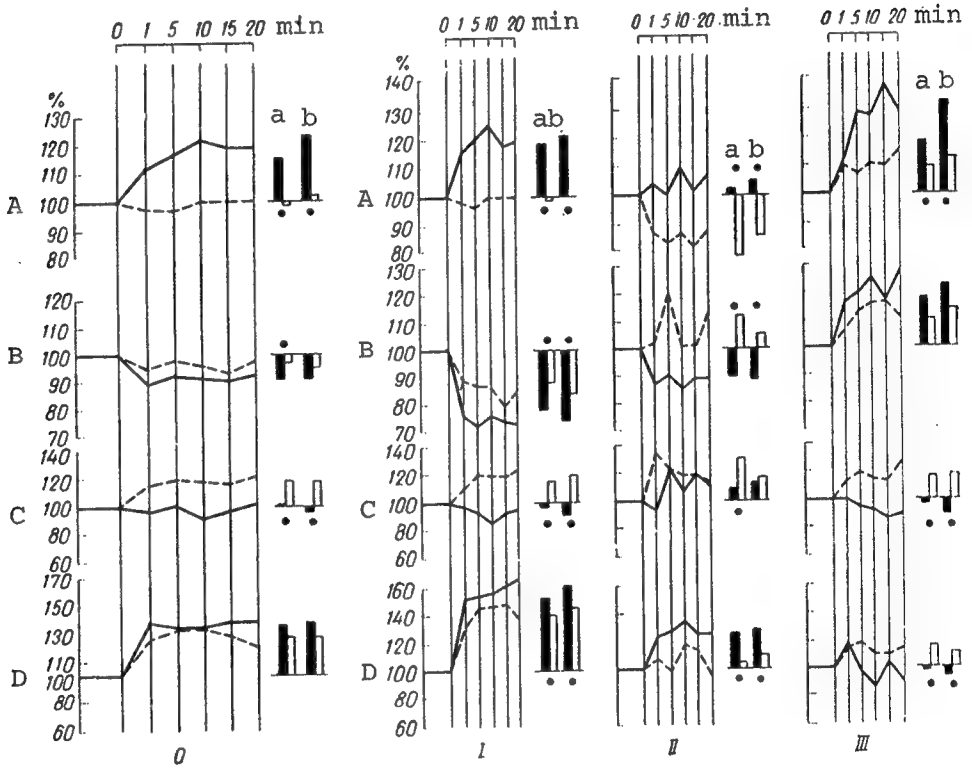


Figure 3. Dynamics of parameters of peripheral hemodynamics in healthy subjects during active (solid lines, black bars) and passive (dash lines, white bars) orthostatic tests

a) transitional period
b) period of stabilized state
A-D) PMFe, PMFv, PRRe and PRRv, respectively

Consistent with the observed changes in PMFv with the first type, vascular resistance increased by 53 and 61% in the different periods of hemodynamic changes during orthostatic tests. This increase was less marked with type II and with the hyperkinetic type PRRv decreased by 2 and 10%, as compared to clinostatic rest.

Less distinct qualitative differences were demonstrable between types of hemodynamic states in the active orthostatic test with regard to changes in blood

flow in muscles of the pelvis and lower extremities. With all types we observed increase in PMFe, which apparently reflected a manifestation of a general condition: increased muscle tone in lower limbs when standing. With respect to the vascular reaction, it should be noted that, while PRRe diminished by 3-13% with types I and III, peripheral vascular resistance increased by 9-12% with type II. This distinction of vascular reactions of lower-limb muscles with the intermediate type is perhaps related to transitional differences in controlling circulation in this hemodynamic state during orthostatic tests. This reaction could be compared to the general direction of changes in parameters of central hemodynamics. The change from a hypokinetic state to an intermediate one during the orthostatic tests is characterized by significant attenuation of manifestation of the orthostatic factor by cardiac output changes, with retention of a rather marked general vascular reactivity (increase of SPR) in orthostatic position and marked systemic increase of peripheral vascular resistance in clinostatic position. Evidently, the increase in regional vascular resistance reflects intensification of constrictor regulation of vascular tonus in intermediate and hyperkinetic states.

Thus, the basic parameters of hemodynamic state during orthostatic tests also differ quite distinctly in regional blood flow characteristics. This correlation is particularly marked for minute blood flow and peripheral resistance of visceral vessels. The direction of change in these parameters corresponds entirely to the typological characteristics of dynamics of cardiac output and total vascular resistance in orthostatic position (see Figure 2). This warrants the assumption that PMFv depends strongly on the state of central hemodynamics. The validity of this conclusion is reinforced by the ratio of regional blood flow to cardiac output. Indeed, there are no differences between all of the hemodynamic states with regard to the PMFv/CI ratio (Figure 4, bottom). In addition to dependence on total cardiac output with all three types of hemodynamic states there is relative increase in blood flow to internal organs when standing. We relate this distinction to "autonomy of regulation" or the evasion phenomenon [5, 9]. This distinction is considerably more marked for circulation, muscles of the pelvis and lower extremities. It is manifested by more marked increase in PMFe/CI than PMFv/CI in the hypokinetic hemodynamic state, i.e., the type with which the orthostatic factor is the most marked.

Considering that the ratio of regional blood flow to cardiac output (PMF/CI) reflects self-regulatory manifestations in the peripheral circulation, we can arrive at the conclusion that, with type I hemodynamic state, in addition to marked manifestation of the orthostatic effect, there is greater functional reactivity of systemic and peripheral mechanisms of vascular regulation of circulation. This is indicated both by the increase in PMF/CI and marked increase in SPR in orthostatic position.

We were impressed by the progressive decline of this reactivity from type I to III (narrowing of hatched area in Figure 4). With type III central hemodynamics in orthostatic position, there is significant decline of regional vascular reactivity. It should also be noted that the change in peripheral vascular reactivity parallels systemic vasoconstriction in increasing the basic vascular tonus at clinostatic rest. The general systemic reaction is characterized by the same direction, which is manifested by less marked increase in SPR in orthostatic position (see Figure 2).

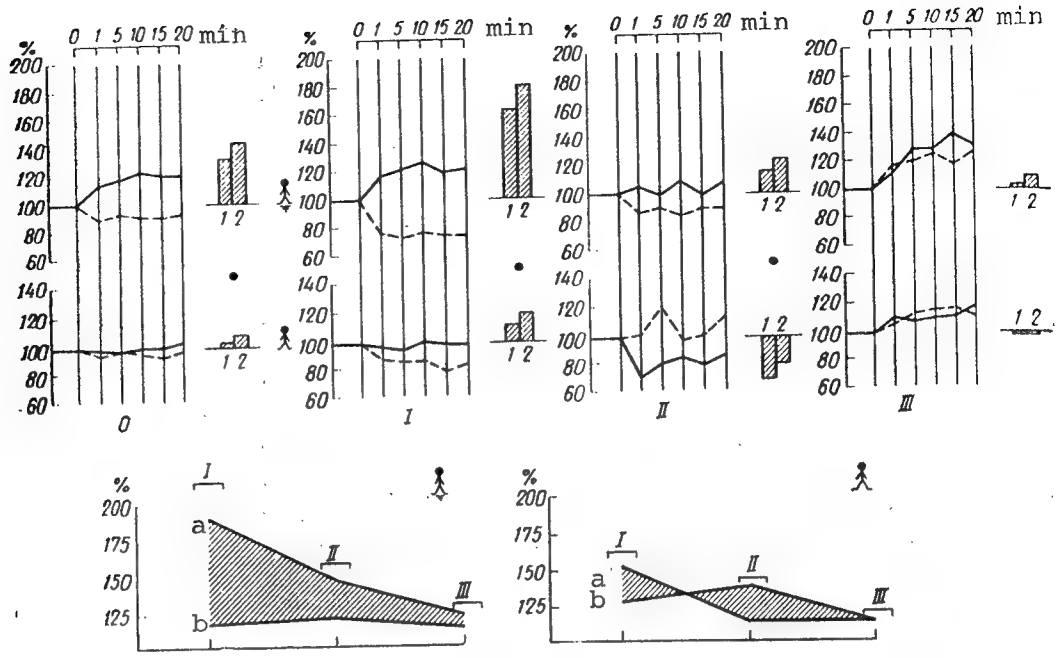


Figure 4. Dynamics of redistribution changes in regional circulation during active (figure with base) and passive orthostatic tests

Top: solid lines, PMFe, dash lines PMFv; hatched bars PMFe/PMFv in 1st-5th and 10th-20th min.
Bottom: typological characteristics of peripheral circulation according to redistribution of minute volume (PMF/CI) in active (left) and passive (right) orthostatic tests. a) PMFe/CI, b) PMFv/CI. The roman numerals indicate type of hemodynamic state. Other explanations given in the text.

Thus, in orthostatic position we see distinct redistribution of the central blood volume in the vascular system of the viscera and muscles of the pelvis and lower extremities. This redistribution is associated with increased blood flow in these regions relative to cardiac output. The redistributional changes are particularly marked in the vascular system of muscles of the pelvis and lower limbs. Such a correlation between regional hemodynamic changes in internal organs and limbs was manifested by increase in parameter of interregional redistribution of blood flow, PMFe/PMFv (see Figure 4). This parameter reveals reliable differences between the basic hemodynamic states during orthostatic tests. The interregional redistribution of blood flow in internal organs and extremities is the most marked with the hypokinetic type (61-78% increase in PMFe/PMFv). With type III hemodynamics, there were virtually no redistribuion changes (PMFe/PMFv increased by only 1-8%). These changes were intermediate in nature with type II.

Considering the fact that the hemodynamic states we distinguished differ qualitatively in characteristics of central and peripheral circulation, we made a comparative analysis of effects of active and passive orthostatic tests for the three distinguished types of hemodynamics.

SI and CI diminished with both the passive and active orthostatic tests over their entire duration in subjects with types I and II hemodynamics (see Figure 2). In contrast, there was relatively minor decline of SI with increase in CI with type III in orthostatic position, which was more marked during active standing. This indicates that there is different manifestation of the orthostatic factor, more marked with types I and II hemodynamic states. Thus, it is expedient to consider expressly these types in making a comparative analysis of hemodynamic effects of passive and active orthostatic tests.

In the transitional period (1-5 min) and at the stage of stabilized hemodynamics, SI and CI diminished more markedly in the active orthostatic test. The most reliable ($P<0.05$) differences in decline of SI and CI were demonstrable in the transitional period, particularly the 1st min of the orthostatic test (see Figure 2). It is important to note that HR was reliably higher in passive orthostatic position, while the velocity of cardiac output did not differ reliably. Consequently, the more marked decline of cardiac output in active orthostatic position cannot be unequivocally related to changes in chronotropic or inotropic function of the heart. In addition, stroke output of the heart during stabilized hemodynamics (10-20 min) in active orthostatic position was relatively higher and related to reliably higher velocity of cardiac output, as compared to passive orthostatic position. This is indicative of greater inotropic stimulation of the heart in this period of active orthostatic position.

The more marked decline of cardiac output in active orthostatic position than in passive is also indicative of more marked redistribution of blood during active standing. Since the latter, unlike passive orthostatic position, is as associated with increase in tonus of antigravity muscles, it can be concluded that the functional efficiency of the muscular pump is limited when standing. It can also be assumed that the decline of cardiac output in active orthostatic position is related to additional redistribution of blood to the vascular system of muscles, particularly those of the pelvic girdle and lower extremities. In addition, the more marked manifestation of the orthostatic factor in active orthostatic position leads to more marked stimulation of compensatory mechanisms in the period of stabilized hemodynamics, and this stimulation is optimal in active orthostatic position, and it is manifested by enhancement of inotropic function of the heart, whereas in passive orthostatic position cardiac compensation of primary hemodynamic changes occurs by intensification of chronotropic function, as manifested by a higher HR.

In view of the foregoing, it is of definite interest to compare the changes in regional blood flow in active and passive orthostatic positions. Examination of the general dynamics of changes in blood flow of internal organs, muscles of the pelvis and lower limbs revealed that, according to the PMFv parameter, there was more marked reduction of visceral blood flow in active orthostatic position than in passive (see Figure 3). Concurrently, there is increase in absolute blood flow in the extremities when standing: by 14% in the transitional period and 20% in the period of stabilized state. In contrast, this parameter (PMFe) is lower in passive orthostatic position, and it increases by only 7 and 1%, respectively.

Considering the fact that the changes in regional blood flow could be related to changes in cardiac output in orthostatic position, one should relate the

changes in regional blood flow to changes in cardiac output for more objective isolation of hemodynamic redistributional changes. This can be done by using the ratios, PMVv/CI and PMFe/CI. In fact, these parameters of peripheral redistribution reflect, as we indicated above, changes in volume of blood flow in the region examined in relation to total minute volume of blood (see Figure 4).

Use of PMFv/CI parameter enabled us to single out more distinctly the actually self-regulatory manifestations of regional hemodynamic changes in abdominal organs in orthostatic position. We found that, with all types of hemodynamic states, there was 15-16% increase in blood flow in orthostatic position, in relation to the general decline of cardiac output, and in passive orthostatic position the increase was more substantial, by 25-26%. Blood flow also increased in the limbs, but these changes were even more prominent in relation to changes in cardiac output according to PMFe/CI. PMFe/CI increased by 51% in the transitional period and by 65% in the period of stabilized hemodynamics. In passive orthostatic position, the increase in blood flow in muscles of the pelvis and limbs was reliably smaller than in active orthostatic position (PMFe/CI increased by only 26 and 37%, respectively).

The different directions of hemodynamic changes in abdominal organs, muscles of the pelvis and lower extremities enable us to assess from the PMVe/PMFv ratio the nature and direction of redistributional changes in the vascular pools of these regions (see Figure 4). The increase in PMFe/PMFv in the transitional period and with stabilized hemodynamics by 31 and 42% in active orthostatic position is indicative of prevalent and marked redistribution of circulation volume in extremital muscles. In passive orthostatic position there was virtually no such redistribution (PMFe/PMFv increased by only 2 and 8%, respectively). It should be noted that this distinction of interregional redistribution was demonstrable in all hemodynamic states during orthostatic tests, but it was the most marked with types I and II.

Our findings confirm our conception [1] of two components of blood redistribution in orthostatic position and the importance of redistribution with a functional or metabolic gradient, which is related to increased tonic strain on muscles of the pelvis and lower limbs during active standing. It is not by chance that it is expressly in active orthostatic position we find substantial and reliable increase in O_2U/CI (see Figure 2), which reflects arteriovenous difference for O_2, as compared to passive orthostatic position. The increase in the latter parameter is indicative of a metabolically more functional state in active orthostatic position. This is also indicated by the somewhat greater O_2 uptake with increased minute volume for the duration of the orthostatic test.

Our findings indicate that with the change from type I to III hemodynamics in orthostatic position, there is decrease in redistributional changes in central and peripheral hemodynamics. This phenomenon occurs against a background of progressive increase in total peripheral resistance of vessels, and it reflects centralization of circulation. The latter is aimed at optimizing central hemodynamics and cerebral circulation in orthostatic position, which is manifested by a drastic reduction of the functional range of changes in cardiac output and vascular tonus in response to orthostatic tests. Such optimization is

obtained by restricting the functional capacities of regulation of peripheral circulation. There is drastic limitation of redistributional hemodynamic changes against a background of systemic vasoconstriction. This is the chief circumstance indicative of the fact that it is expressly in a hyperkinetic state that there is complete elimination of hemodynamic differences between parameters of active and passive orthostatic position.

The more marked decline of cardiac output in active orthostatic position, which is related to hydrostatic and functional redistribution of blood, also causes more marked systemic vasoconstriction intensification of inotropic function of the heart during active standing than in the passive test. However, the persisting redistribution of blood, particularly to vessels of the lower limbs, so to speak decentralizes hemodynamics. For this reason, the increase in total vascular resistance is associated with only moderate elevation of BPm, whereas in passive orthostatic position there is relatively less decline of cardiac output against the background of systemic vasoconstrictive reaction, which overlaps regional redistribution and is reflected by reliably greater elevation of BPs, BPd and BPm, than in active orthostatic position.

The more distinct differences in regional redistribution of blood flow with active and passive orthostatic tests (to internal organs and lower extremities), as compared to changes in central hemodynamics, are indicative of the great importance of regulation of peripheral circulation to compensation of orthostatic changes in hemodynamics. The redistribution of blood in the vascular systems of internal organs and muscles modifies and nullifies differences, to a significant extent, in changes in central hemodynamics during the active and passive forms of orthostatic tests and, in spite of the significant decline of minute blood volume, provides for the required blood flow level for actively functional muscles during standing and blood supply to the viscera.

BIBLIOGRAPHY

1. Belkaniya, G. S., KOSMICHESKAYA BIOL., No 6, 1981, pp 4-9.

2. Idem, "Problemy kosmicheskoy biologii. T. 45. Funktsional'naya sistema antigravitatsii" [Problems of Space Biology. Vol 45: Functional Antigravity System], Moscow, 1982.

3-4. Dartsmeliya, V. A. and Belkaniya, G. S., KOSMICHESKAYA BIOL., No 1, 1983, pp 85-86.

5. Johnson, P., "Peripheral Circulation," Moscow, 1982.

6. Yelizarova, N. A., Bitar, S., Aliyeva, G. E. et al., TER. ARKH., No 12, 1981, pp 16-21.

7. Osadchiy, L. I., "Polozheniye tela i regulyatsiya krovoobrashcheniya" [Body Position and Regulation of Circulation], Leningrad, 1982.

8. Pushkar', Yu. T., Bol'shov, V. M., Yelizarova, N. A. et al., KARDIOLOGIYA, No 7, 1977, pp 85-89.

9. Khayutin, V. M., "Vasomotor Reflexes," Moscow, 1964.

10. Chazov, Ye. I., ed., "Rukovodstvo po kardiologii" [Manual of Cardiology], Moscow, Vol 2, 1982, pp 9-138.

11. Goldwater, D., Montgomery, K., Hoffler, G. W. et al., in "Aerospace Medical Association. Annual Scientific Meeting," Washington, 1979, pp 51-52.

12. Spodick D. H. and Lance, V. Q., AVIAT. SPACE ENVIRONM. MED., Vol 48, 1977, pp 432-433.

13. Stevens, P. M., AM. J. CARDIOL., Vol 17, 1966, pp 211-218.

14. Ward, R. J., Danziger, F., Bonica, J. J. et al., AEROSPACE MED., Vol 37, 1966, pp 257-259.

UDC: 616.153.466-02:612.766.2]-07

AMINO ACID COMPOSITION OF HUMAN BLOOD SERUM DURING IMMERSION HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 15 Jul 83) pp 39-41

[Article by A. S. Ushakov, T. F. Vlasova and Ye. B. Miroshnikova]

[English abstract from source] The content of free amino acids was measured in the blood serum of 6 male test subjects exposed to 7-day immersion. During the study the concentration of amino acids decreased in a different manner typical of a stress-effect. The results obtained can be used to develop a system of prevention and therapy of amino acid unbalance.

[Text] Numerous studies of recent years indicate that both spaceflight factors and their simulation on the ground lead to changes in parameters of amino acid metabolism, the severity of wich depends on duration, as well as nature of factor eliciting redistribution of the amino acid pool [1, 2, 5-12, 18, 19]. There are no data in the literature concerning amino acid metabolism during immersion hypokinesia. We submit here the results of a study of the blood amino acid pool under the influence of this factor.

Methods

We used the model of "dry" immersion [14] as a factor simulating one of the chief effects of spaceflights, weightlessness. The tests were conducted in a special tank 200×100×100 cm in size. A sheet of waterproof film was placed on the surface of the tank, and it was of the same size as the tank. This sheet of film served as a barrier separating the subject from the liquid. Water temperature in the tank was kept at 33±0.5°C. The subject was immersed in the tank up to his neck, in horizontal position.

The daily schedule consisted of 8-h sleep, 3 meals consisting of a controlled diet, a program of clinical and physiological tests and personal time (watching television, reading, keeping diaries). We tested 6 healthy men 25 to 35 years of age. The subjects were submitted to immersion hypokinesia for 7 days.

We analyzed free amino acids (FA) in the subjects' blood serum using an automatic analyzer with ion-exchange chromatography [3, 16]. Venous blood was drawn on a fasting stomach on the 2d, 4th and 6th days of the experiment. The samples of blood serum were deproteinized with sulfosalicylic acid prior to analysis [15].

Free amino acid levels (mg%) in subjects' blood serum during immersion, M±m

Amino acids	Background ($n=5$)	Water immersion, days					
		2 ($n=6$)	P	4 ($n=6$)	P	6 ($n=6$)	P
Isoleucine	0,63±0,10	0,60±0,06	>0,1	0,55±0,07	>0,1	0,72±0,06	>0,1
Leucine	1,29±0,16	1,31±0,12	>0,1	1,16±0,14	<0,1	1,18±0,07	>0,1
Valine	2,26±0,11	1,84±0,10	<0,05	1,82±0,16	<0,05	1,90±0,09	>0,05
Threonine	3,30±0,11	2,29±0,16	<0,001	2,45±0,32	<0,05	2,38±0,18	<0,02
Serine	1,29±0,08	1,19±0,13	>0,1	1,04±0,19	>0,1	1,09±0,08	>0,1
Methionine	0,25±0,04	0,35±0,06	>0,1	0,26±0,03	>0,1	0,27±0,03	>0,1
Tyrosine	0,70±0,08	0,66±0,10	>0,1	0,69±0,13	>0,1	0,69±0,27	>0,1
Phenylalanine	0,64±0,06	0,59±0,08	>0,1	0,65±0,19	>0,1	0,64±0,09	0
Cystine	0,32±0,03	0,30±0,06	>0,1	0,34±0,04	>0,1	0,32±0,07	0
Aspartic acid	0,15±0,02	0,10±0,01	<0,05	0,18±0,03	>0,1	0,12±0,02	>0,1
Glutamic acid	2,56±0,34	3,17±0,38	>0,1	2,71±0,34	>0,1	2,37±0,15	>0,1
Proline	2,29±0,15	1,92±0,44	>0,1	1,75±0,20	>0,05	2,14±0,33	>0,1
Glycine	1,32±0,17	1,37±0,13	>0,1	1,16±0,10	<0,1	1,26±0,09	>0,1
Alanine	3,17±0,22	2,49±0,21	<0,05	2,01±0,09	<0,01	2,30±0,26	<0,05
Sum of 14 amino acids	20,2	18,2		16,2		17,4	

Results and Discussion

The data obtained in the course of this study concerning amino acid composition in the subjects in the background period and on the 2d, 4th and 6th days of water immersion are listed in the Table. Blood serum FA content in the background period was virtually the same as the physiological norm, and for this reason we compared all of the experimental results to background data. As can be seen in the Table, there was selective decline of FA in blood serum on the 2d day of immersion hypokinesia: valine ($P<0.05$), threonine ($P<0.01$), aspartic acid ($P<0.05$) and alanine ($P<0.05$). On the 4th and 6th days, the amino acid spectrum did not change and valine, threonine and alanine remained at the same low level. Thus, water immersion elicited a differentiated decline of FA in human blood serum and this, in turn, was reflected in their overall content. On the 2d, 4th and 6th days, the total amino acid pool constituted 18.2, 16.2 and 17.4 mg%, respectively, which is somewhat less than in the background period--20.2 mg%. In essence, the reduction of the pool occurred at the expense of nonessential amino acids. Evidently, the demonstrated shift of amino acid equilibrium was due to the increased valine, aspartic acid and alanine requirements during the hypokinetic period and their utilization for the anabolic needs of the body. On the basis of the existing data in the literature [1, 2, 5-12, 18, 19], which were obtained both after spaceflights and in ground-based experiments with simulation of spaceflight, it can be maintained that the conditions of 7-day water immersion elicit stressogenic changes. Amino acid metabolism reacts to a stress factor by distinctive redistribution of the amino acid pool, in particular, its decline in blood. Such a decline is, of course, consistent with conventional conceptions of the physiological role of free amino acids as the body's reserve, utilization of which during a stress period increases against the background of diminished intensity of biosynthetic processes [13]. Expressly at this moment, the question arises of instituting

preventive measures to restore amino acid balance. For this reason, our findings concerning the blood serum amino acid spectrum could be useful in elaborating therapeutic and preventive measures. It is necessary to mention that the body's protein supply can be assessed on the basis of blood valine level, as indicated by the data of Swendseid et al. [17] and V. G. Vysotskiy et al. [4]. For this reason, the demonstrated decline of valine concentration in the course of our experiment could also have been due to a nutritional imbalance. Evidently, the decline of aspartic acid and threonine levels in the subjects' blood serum was due to their active involvement in processes of energy production and, finally, active participation of aspartic acid and alanine in transamination.

Thus, in the course of our investigation it was demonstrated that the factor used (immersion hypokinesia) elicits certain changes in the subjects' blood amino acid status. The demonstrated dynamics of blood amino acid composition are indicative of change in anabolic processes during the period of adaptation to immersion hypokinesia.

BIBLIOGRAPHY

1. Bychkov, V. I., Borodulina, I. I. and Vlasova, T. F., KOSMICHESKAYA BIOL., No 5, 1981, pp 21-23.

2. Vlasova, T. F., Miroshnikova, Ye. B., Ushakov, A. S. et al., Ibid, No 4, 1978, pp 23-27.

3. Vysotskiy, V. G., Vlasova, T. F. and Ushakov, A. S., LAB. DELO, No 9, 1973, pp 570-572.

4. Vysotskiy, V. G., Vlasova, T. F., Ushakov, A. S. et al., VOPR. PITANIYA, No 2, 1974, pp 16-19.

5. Nevolina, T. V., Polyakov, V. V. and Vlasova, T. F., in "Aktual'nyye voprosy kosmicheskoy biologii i meditsiny" [Pressing Problems of Space Biology and Medicine], Moscow, 1975, Vyp 2, pp 154-155.

6. Polyakov, V. V., Agureyev, A. N., Vlasova, T. F. et al., KOSMICHESKAYA BIOL., No 1, 1977, pp 43-47.

7. Popov, I. G. and Latskevich, A. A., Ibid, No 2, 1982, pp 14-19.

8. Idem, Ibid, No 1, 1983, pp 15-21.

9. Idem, Ibid, No 2, pp 23-30.

10. Idem, Ibid, No 3, pp 23-29.

11. Ushakov, A. S., Vlasova, T. F., Miroshnikova, Ye. B. et al., Ibid, No 1, pp 10-15.

12. Ushakov, A. S. and Vlasova, T. F., in "Fiziologicheskiye i klinicheskiye problemy adaptatsii cheloveka i zhivotnogo k gipotermii, gipoksii i gipodinamii" [Physiological and Clinical Problems of Human and Animal Adaptation to Hypothermia, Hypoxia and Hypodynamia], Moscow, 1975, pp 149-150.

13. Fedorov, I. V., KOSMICHESKAYA BIOL., No 3, 1980, pp 3-10.

14. Shul'zhenko, Ye. B., "Physiological Effects of Altered Gravity," author abstract of doctoral dissertation, Moscow, 1975.

15. Hamilton, P. B., ANN. N.Y. ACAD. SCI., Vol 102, 1962, pp 55-75.

16. Spackman, D. H., Stein, W. H. and Moore, S., ANALYT. CHEM., Vol 30, 1958, pp 1190-1203.

17. Swendseid, M. E., Tuttle, S. G., Figueroa, W. S. et al., J. NUTR., Vol 88, 1966, pp 239-248.

18. Ushakov, A. S. and Vlasova, T. F., AVIAT. SPACE ENVIRON. MED., Vol 47, 1976, pp 1061-1064.

19. Idem, LIFE SPACE RES., Vol 14, 1976, pp 256-262.

UDC: 616.153.915-02:612.766.2]-07

EFFECT OF LONG-TERM HYPOKINESIA ON BLOOD SERUM LIPID SPECTRUM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 15 Jul 83) pp 42-45

[Article by I. L. Medkova, K. V. Smirnov, V. P. Naydina, B. L. Avetisyants and Yė. Ye. Zharkovskaya]

[English abstract from source] The effect of 120-day head-down tilt on the lipid spectrum of blood serum was investigated. By thin-layer and gas liquid chromatography lipids (total lipids, phospholipids, cholesterol and its esters, nonesterified fatty acids, triglycerides) and higher fatty acids were identified. It was found that cholesterolemia increased at the expense of the ester bound fraction, phospholipids decreased drastically, the ratio of phospholipids to total cholesterol decreased, and triglyceridemia diminished. Until bed rest day 70 saturated fatty acids were predominant, with linoleic acid being deficient, and thereafter the relative content of unsaturated fatty acids increased. The above changes in the lipid spectrum can be considered as risk factors with respect to preclinical stages of atherosclerosis.

[Text] Investigation of lipid metabolism under hypokinetic conditions has attracted many researchers. In animal experiments, authors have demonstrated hypercholesterolemia, increased lipolysis, which leads to mobilization of fat from the fatty reservoirs and increase in concentration of nonesterified fatty acids (NEFA) in blood [7, 9, 10]. Studies of humans kept on strict bed-rest for a long period of time also revealed elevated levels of cholesterol, total lipids and β-lipoproteins in blood [2].

Present use of chromatographic analysis (thin-layer and liquid-gas) makes it possible to broaden the range of tested parameters of lipid composition of blood serum. It is possible to examine the distribution of lipids according to classes of compounds (total lipids, phospholipids, cholesterol and its esters, monoglycerides, diglycerides, triglycerides, NEFA), on the one hand, and composition of fatty acids (FA) of blood serum with different number of carbon atoms and saturation, on the other.

Our objective here was to examine the blood serum lipid spectrum using thin-layer chromatography and the composition of FA with liquid-gas chromatography on people at different stages of long-term bedrest.

Methods

We had 6 essentially healthy men, 30 to 40 years of age, on strict bedrest in antiorthostatic [head-down tilt] position (angle of tilt -4.5°) for 120 days. Blood was drawn in the background period, on the 28th, 49th, 70th, 95th, 112th days of hypokinesia, 7th and 14th days of the recovery period. Serum lipids were extracted according to Folch [12]. The lipid spectrum was identified by thin-layer chromatography on Silufol plates [6]. We used a system consisting of hexane, diethyl ether and glacial acetic acid in a proportion of 80:20:20 to separate lipids into classes of compounds. For better demonstration of lipid fractions, after separation the plates were placed in iodine fumes for several seconds. Then they were sprayed with 0.04% alkaline alcohol solution of bromocresol green, after which they were dried for 1 min at 100°C. The plates were then treated sith 10% alcohol solution of phosphomolybdenic acid and again incubated for 4 min at 100°C. Quantitative assay of lipid spots was performed by the densitometry method on an ERI-50 instrument of the Karl Zeiss firm, using appropriate standards--free cholesterol, cholesterol esters, triolein, mixture of phospholipids, mixture of free fatty acids (FFA) (Serva firm, FRG).

The fatty acid composition of total lipids of blood serum was analyzed by gas-fluid chromatography on a Tsvet-100 chromatograph with flame-ionization detector and glass column; the length of the column was 3.6 m and inside diameter 4 mm; chromium Q was the gas filler with a liquid phase of 5% DEGS. Column temperature 180%C and evaporator temperature 220°C. We analyzed the methyl esters of FA of total lipids obtained with use of tetramethylammonium hydroxide (TMA•OH) and methyl iodide [4].

Lipids were extracted from 0.1 mℓ serum using isopropyl alcohol (3 times 0.5 mℓ each time). The combined extracts were dried in a flow of nitrogen, we then added 0.5 mℓ 12% TMA•OH solution mixed with methanol and isopropanol (1:1), the vials were heated to 230°C (1-2 min), the solution was vaporated to 1/2 its volume, then cooled and we added 0.4 mℓ methyl iodide; the solution separated into layers when slightly shaken. The bottom layer was collected in a syringe and 0.4 mℓ methyl iodide was again added. The combined solutions of methyl esters were evaporated in a flow of nitrogen, and the dry residue was dissolved in 20 μℓ carbon tetrachloride. The obtained solution (2 μℓ) was introduced in the gas chromatograph. Quantitative evaluation of relative amounts of higher FA (percentage) by the method of internal normalization [11] was made from the chromatograms of methyl esters of fatty acids.

Results and Discussion

The investigations revealed that there was insignificant change in concentration of total lipids of blood serum throughout the hypokinetic period. We observed only once a reliable increase in total lipid content on the 70th day of hypokinesia. Substantial changes were demonstrated in dynamics of total cholesterol, chiefly referable to the ester-bound fraction. Already on the 28th day of the study, blood cholesterol ester concentrations began to increase reliably (Figure 1). With extension of the hypokinetic period these changes became marked. Thus, on the 49th day cholesterol esters of blood serum constituted 278.5 mg% (background 157.0 mg%, $P<0.002$), on the 70th day 292.9 mg% ($P<0.001$),

on the 112th day 229.9 mg% ($P<0.05$). On the 7th day of the recovery period, cholesterol ester levels in blood constituted 312.4 mg% ($P<0.001$), which was almost twice the background value. The coefficient characterizing the ratio of cholesterol esters to total cholesterol constituted 0.93 in the background period, and it rose to 1.31 with extention of the period of restricted motor activity.

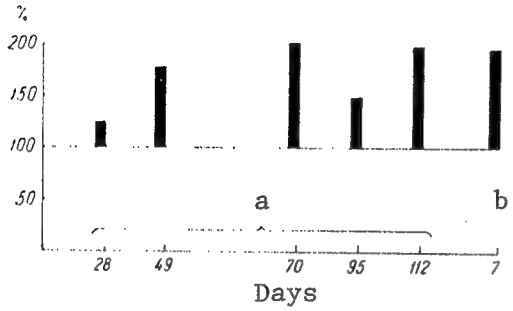


Figure 1.
Cholesterol ester concentrations (% of background). Here and in Figure 2:
a) hypokinesia
b) recovery period

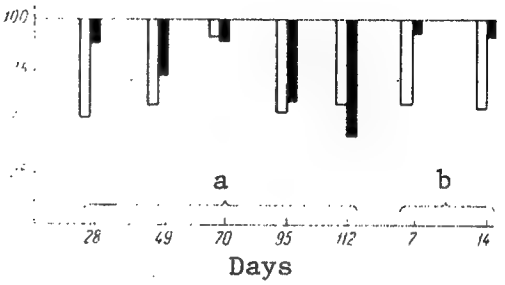


Figure 2.
Phospholipids and triglycerides (% of background)
White bars, phospholipids; black, triglycerides

There was phasic change in concentration of NEFA during hypokinesia, but it was not reliable.

Substantial changes were noted in dynamics of phospholipids (Figure 2), the levels of which in blood serum dropped drastically and reliably during hypokinesia and in the recovery period. Hypophospholipidemia, along with hypercholesterolemia, led to significant (to 1/2 or more) decline of the coefficient characterizing the ratio of phospholipids to total cholesterol.

During this study we found a decline in concentration of blood serum triglycerides (see Figure 2), which was the most marked toward the end of the hypokinetic period (95th and 112th days). This parameter differed insignificantly in the recovery period from background values.

Thus, these data indicate that cholesterol and phospholipids were the most vulnerable classes of lipids during 120-day antiorthostatic hypokinesia (AOH).

Examination of the spectrum of higher FA of total lipids of blood serum revealed several substantial changes during 120-day AOH (see Table). We found progressive increase, with increase in duration of hypokinesia, in percentage of palmitoleic acid ($C_{16:1}$), which was reliable at all tested times. The level of palmitic acid ($C_{16:0}$) changed insignificantly during hypokinesia. Stearic acid ($C_{18:0}$) content had a tendency toward decline, and reliable changes were demonstrable toward the end of the hypokinetic period (95th and 112th days). In addition, oleic acid ($C_{18:1}$) content increased in the course of the study (reliably on the 112th day of bedrest). Appreciable changes were found in level of unsaturated linoleic acid ($C_{18:1}$)--reliable decline on the 28th and 70th days followed by increase to almost the background level toward the end

of the study. The shortage of metabolically active linoleic acid on the 28th a and 70th days of hypokinesia was reflected by coefficient K_2, the ratio of oleic acid to linoleic acid, which was highest at expressly these times. Subsequently, with increase in duration of bedrest, the percentage of linoleic acid reverted to the base value, along with compensatory increase in monounsaturated oleic acid. This, in turn, resulted in a higher value for K_2 on the 95th and 112th days of hypokinesia, as compared to the background.

Higher fatty acids of blood serum (in rel.%) during 120-day hypokinesia, M±m (n = 6)

Code name for fatty acid	Background	Day of hypokinesia			
		28	70	95	112
16:0	27,1±0,6	28,9±0,6 (<0,05)	31,2±0,6 (<0,001)	27,2±2,3 (>0,1)	27,7±0,5 (>0,1)
16:1	4,1±0,2	6,8±0,3 (<0,001)	5,5±0,5 (<0,05)	6,8±0,3 (<0,001)	7,1±0,4 (<0,001)
18:0	10,4±0,5	9,9±0,4 (>0,1)	9,4±0,7 (>0,1)	6,9±0,4 (<0,001)	6,0±0,6 (<0,001)
18:1	31,6±1,2	30,8±1,7 (>0,1)	34,4±1,1 (>0,1)	34,6±1,3 (>0,1)	35,5±0,9 (<0,05)
18:2	25,8±0,9	19,9±0,8 (<0,001)	18,5±1,4 (<0,002)	24,5±0,9 (>0,1)	23,8±1,0 (>0,1)
$K_1 = \frac{\text{Total SFA}}{\text{Total USFA}}$	0,61	0,67	0,70	0,52	0,51
$K_2 = \frac{18:1}{18:2}$	1,22	1,55	1,86	1,41	1,49
$K_3 = \frac{\text{Total USFA}}{18:2}$	1,45	1,95	2,19	1,39	1,42
$K_4 = \frac{\text{Total SFA + total mono USFA}}{18:2}$	2,83	3,84	4,35	3,08	3,21

Note: P is given in parentheses.

With regard to the FA spectrum, it can be noted that the sum of saturated fatty acids (SFA) was greater than the sum of unsaturated ones (USFA: K_1 and K_3) up to the 70th day of hypokinesia, whereas on the 95th and 112th days, on the contrary, there was prevalence in blood of metabolically more active USFA.

In discussing the results, we must dwell on the physiological implications of different classes of lipids and FA.

We know of the role of phospholipids and cholesterol as biologically active substances involved in building the membrane structures of organs and tissues. In addition, cholesterol is the source of synthesis of biologically active substances with a sterol nucleus, hormones, vitamins and bile acids. It is also known that a rise in blood cholesterol level with drastic decline of phospholipid concentrations causes an unfavorable correlation between these components, which are instrumental in precipitation of cholesterol in solution and deposition in the vascular intima, and this leads to atherosclerotic changes in the vascular bed [1]. Hypercholesterolemia is one of the main "high risk factors" in development of atherosclerosis. Tests using cholesterol labeled with radioactive isotopes revealed that virtually all of the

cholesterol in the region of atherosclerotic regions gets there from plasma [8], and the higher the phospholipids/cholesterol ratio (which normally equals 1), the lower the probability of development of atherosclerotic changes [3].

In our study, during hypokinesia we observed significant increase in blood cholesterol ester concentrations, with drastically lowered phospholipid levels, which led to substantial decline of the phospholipids/cholesterol coefficient (0.28 on the 95th day of hypokinesia, 0.37 on the 7th day of the recovery period; 0.85 in the background period). Our findings confirm the theses in the literature to the effect that the changes demonstrated during hypokinesia are identical to those found with atherosclerosis [9]. The opinion is held that, aside from elevation of blood cholesterol level, elevation of total lipid and blood serum triglyceride levels are important risk factors for development of atherosclerosis. In our studies, we found virtually no increase in concentration of total lipids (with the exception of the 70th day of hypokinesia), while triglyceride levels even dropped during the period of restricted motor activity. However, as indicated by A. A. Dzizinskiy and V. P. Puzyrev [5], a normal level of total lipids of blood does not necessarily rule out the danger of atherosclerosis, particularly when other risk factors are present.

Investigation of the spectrum of fatty acids of total lipids revealed that there was prevalence of SFA in blood up to the 70th day of hypokinesia. Maximum changes were demonstrated in linoleic acid content, the level of which dropped noticeably on the 28th-70th days of hypokinesia. It is mentioned in the literature that there is a substantial decrease in relative amounts of USFA (particularly distinct on the example of linoleic acid) in patients with atherosclerosis [1]. On the other hand, it is known that blood serum cholesterol content decreases expressly under the influence of polyunsaturated fatty acids [8]. These data are indicative of the similarity of demonstrated changes in lipid composition of blood serum during hypokinesia and those seen with atherosclerosis (apparently at the preclinical stages). However, by the end of the hypokinetic period (95th and 112th days), the spectrum of FA revealed increase in relative amount of unsaturated forms, which is apparently a favorable factor and indicative of the compensatory nature of some of the demonstrated changes.

BIBLIOGRAPHY

1. Alimova, Ye. K., Astvatsatur'yan, A. T. and Zharov, L. V., "Lipidy i zhirnyye kisloty v norme i pri ryade patologicheskikh sostoyaniy" [Lipids and Fatty Acids Under Normal Conditions and in Several Pathological States], Moscow, 1975, pp 237-258.

2. Bychkov, V. P., Borodulina, I. I., Gryaznova, V. N. et al., in "Chteniya, posvyashch. razrabotke nauchnogo naslediya i razvitiyu idey K. E. Tsiolkovskogo , 5-ye. Trudy" [Transactions of 5th Series of Lectures Dedicated to Development of the Scientific Legacy and Ideas of K. E. Tsiolkovskiy], Moscow, 1971, p 132.

3. Parsons, D., "Biological Membranes," Moscow, 1978, p 25.

4. Vatulya, N. M., Karmen, I. P., Naydina, V. P. et al., LAB. DELO, No 4, 1980, pp 211-213.

5. Dzizinskiy, A. A. and Puzyrev, V. P., "Nasledstvennost' i ateroskleroz" [Heredity and Atherosclerosis], Novosibirsk, 1977.

6. Kirkhner, Yu., "Tonkosloynaya khromatografiya" [Thin-Layer Chromatography], Moscow, Vol 2, 1981, pp 52-106.

7. Lobova, T. M., KOSMICHESKAYA BIOL., No 5, 1973, pp 32-35.

8. Newman, E. V., Paul, O., Blumenthal, S. et al., in "Atherosclerosis," Moscow, 1975, pp 40-124.

9. Potapov, P. P., "Glycosaminoglycans (Mucopolysaccharides), Collagen and Lipids of Tissues During Hypodynamia," author abstract of candidatorial dissertation, Moscow, 1978.

10. Ryl'nikov, Yu. P., KOSMICHESKAYA BIOL., No 2, 1974, pp 8-13.

11. Stolyarov, B. V., Savinov, I. M. and Vitenberg, A. G., "Rukovodstvo k prakticheskim rabotam po gazovoy khromatografii" [Manual of Gas Chromatography], Leningrad, 2d. ed., 1978, pp 199-203.

12. Folch, J., Lees, M. and Sloane, Stanley G. H., J. BIOL. CHEM., Vol 226, 1957, p 497.

UDC: 616-005.1-036.18-085.38-07:616.13/.14-
008.1+616.24-008.7-092:612.766.2.014.477

DISTINCTIVE CHANGES IN REGIONAL HEMODYNAMICS AND GAS EXCHANGE IN HEALTHY MAN IN RESPONSE TO MODERATE PHLEBOTOMY AND REINFUSION OF BLOOD AFTER SUBMITTING TO ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 25 Jul 83) pp 45-48

[Article by V. Ye. Vorob'yev, I. B. Goncharov, I. V. Kovachevich and A. F. Davydkin]

[English abstract from source] Nine healthy male test subjects were exposed for 7 days to head-down tilting. Within 2 hours after exposure 500 ml of blood were withdrawn. This reduced pulse blood filling of all lung compartments, particularly the upper ($P<0.05$) compartments, and decreased slightly finger circulation. The blood losses were then substituted but 2 hours after blood reinfusion the rheographic parameters of pulmonary circulation were still lower than before blood losses. In arterial blood pCO_2 remained lower ($P<0.05$) and the deficiency of bases increased ($P<0.05$). It can be concluded that in the above situation blood reinfusion in the amount exceeding blood losses should be viewed adequate. On the basis of the results obtained increased blood content of the lungs in the course of head-down tilt can be interpreted as a reflex mechanism of blood pooling in the body.

[Text] It is known that antiorthostatic hypokinesia [head-down tilt] (AOH) leads to reduction of circulating blood volume in healthy man with concurrent increase in filling of the intrathoracic region.

However, the mechanism of such plethora of the lungs has not been definitively identified. It can be viewed as stasis occuring as a result of redistribution of blood [4] or because the pulmonary vessels serve as a reservoir for blood that is "superfluous" under antiorthostatic conditions and collects there for potential use by the body when circulation changes.

Our objective here was to make a combined study of regional hemodynamics and exchange of gases in response to controlled bloodletting and blood replacement in subjects submitted previously to AOH.

Methods

External respiration, gas composition and acid-base balance (ABB) of arterial blood were studied in 9 essentially healthy subjects in the first 2 h of the recovery period following 7 days in antiorthostatic position at an angle of -8°. Gas composition of exhaled air was analyzed using a capnograph and paramagnetic oxygen analyzer. Samples of arterial blood drawn by puncturing the radial artery were immediately analyzed by the Astrup method in an AME-1 instrument [6].

Concurrently, using a 4RG-1A rheograph and Galileo encephalograph we recorded rheograms from the upper, middle and lower parts of the right lung, as well as finger by the conventional method [1]. We studied the following parameters: α/T, which reflects tonus and elasticity of large and medium caliber arteries; dicrotic (DCI) and diastolic (DSI) indexes, which reflect tonus of arterioles and veins, respectively; we calculated the parameter of intensity of pulsed delivery of blood (RI) in vessels of the tested region. According to the method of V. G. Shershnev et al. [3], to record rheograms of the pulmonary artery, the first electrode, 2.5×3.0 cm in size, was placed over the second intercostal pace, between the peristernal line and midclavicular line, and the second electrode, 6.0×10.0 cm in size, was placed below the bottom angle of the scapula.

Immediately after termination of AOH and moving the subjects to horizontal position, we drew 500 mℓ blood in 15 min through a subclavian catheter, the tip of which was in the superior vena cava, by means of a roller pump, into an 0.5 ℓ vial. The subclavian vein was catheterized under local anesthesia (0.25% novocain). In this period, we did not replace the removed volume with blood substitutes. We began to reinfuse the blood at a volumetric rate of 100 mℓ/min 15 min after bloodletting. All tests were performed with the subjects lying down. The obtained results were submitted to statistical processing. Reliability of differences was assessed using Student's criterion.

Results and Discussion

In the background tests prior to AOH all of the parameters studied were in the normal range.

Rheograms taken just prior to bloodletting failed to demonstrate significant changes in blood supply to the lower parts of the lungs or finger (Table 1). Analysis of rheograms of the upper and middle compartments of the lungs revealed absence of dicrotic notch in five subjects. Disappearance of the dicrotic notch was indicative of a tendency toward increased vascular tonus in the tested region. The latter can be interpreted as a compensatory-adaptive reaction for better intrapulmonary distribution of the increased volume of blood, which is present under AOH conditions.

At the same time, there was a tendency toward increased CO_2 tension (pCO_2) and decrease of O_2 tension (pO_2) (Table 2), with regard to gas composition of blood. We also demonstrated a tendency toward increase in arterial-alveolar gradient for oxygen ($p_{A-a}\ O_2$).

Table 1. Dynamics of rheographic parameters during bloodletting and after replacement of blood, M±m

Region examined	Parameter	Period of study		
		before phlebotomy	at height of blood loss	2 h after blood replacement
Top part of lungs	RI, relative units	1,79±0,31	1,15±0,33*	1,95±0,02
	DCI, %	—	—	—
	DSI, %	—	—	—
	α/T, %	24,54±1,83	21,68±1,15	22,89±1,93
Middle part of lungs	RI., relative units	1,51±0,22	1,08±0,24	1,20±0,22
	DCI, %	—	—	—
	DSI, %	—	—	—
	α/T, %	22,18±1,61	27,61±2,59	29,87±0,43*
Bottom part of lungs	RI, relative units	1,16±0,42	1,02±0,26	0,82±0,07
	DCI, %	60,0±15,20	86,25±6,19	85,0±6,45
	DSI, %	70,5±14,79	103,75±11,52	90,0±9,12
	α/T, %	24,99±3,18	24,35±5,67	25,95±6,61
Pulmonary artery	RI, relative units	2,50±0,53	1,39±0,51*	1,87±0,64
	α/T, %	19,38±1,79	26,54±2,83*	33,25±1,19*
Finger	RI, relative units	1,48±0,31	1,11±0,19	0,77±0,07*
	DCI, %	36,25±5,11	28,45±4,43	45,20±12,15
	DSI, %	50,50±7,27	44,35±3,02	61,86±13,45
	α/T, %	10,15±0,42	10,25±0,64	17,30±5,65

Note: Here and in Table 2, the asterisk shows reliability of differences from background, prior to phlebotomy at $P<0.05$.

Table 2. Dynamics of some parameters of external respiration and blood ABB with phlebotomy and replacement of blood, M±m

Parameter	Period of study			
	before AOH	before phlebotomy	at height of blood loss	2 h after blood replacement
RR/min	12,3±1,49	12,9±1,49	12,5±1,24	14,7±1,37
p_AO_2, mm Hg	104,4±1,50	103,6±2,62	100,3±2,82	103,0±3,45
p_ACO_2, mm Hg	38,7±1,58	37,6±1,33	34,0±2,09	35,6±1,90
pH	7,424±0,01	7,422±0,01	7,380±0,02	7,390±0,01
SB, mmol/ℓ	25,2±0,15	25,3±0,46	23,4±0,68	22,3±0,51*
BE, mmol/ℓ	0,9±0,26	+1,3±0,50	—1,1±0,78	—2,7±0,67*
p_aCO_2, mm Hg	38,3±1,31	38,7±0,38	35,8±1,14	35,3±0,84*
p_aO_2, mm Hg	94,3±1,69	85,9±3,78	83,6±5,38	84,5±5,90
$p_{A-a}O_2$, mm Hg	8,1±3,10	20,8±2,70	21,6±3,84	19,2±3,62

Key: RR) respiration rate

Drawing 500 mℓ blood led to some decrease in intensity of pulsed filling of all parts of the lungs, and this was reliable for the upper compartments ($P<0.05$). With regard to blood gases, the subjects presented a tendency toward decline of pCO_2 and pO_2, as well as a tendency toward increased shortage of bases (BE) and standard bicarbonates (SB) in ABB of blood.

According to the literature [1, 7], impaired hemodynamics in the systemic and pulmonary circulatory systems are the chief cause of changes in gas exchange with loss of blood. Moreover, in the opinion of several researchers [2, 5], a reduction of total blood volume leads to significant discharge of a certain amount of blood from the pulmonary vascular system. The postphlebotomy reduction of blood volume is more marked in the lungs than skeletal muscles.

The validity of this thesis for our experimental conditions is also confirmed by data on delivery of blood to the pulmonary artery, which are indicative of significant ($P<0.05$) reduction. At the same time, we found an increase in tonus of the pulmonary artery wall, apparently compensatory in nature. There was also insignificant decrease in intensity of circulation in the subjects' finger against a background of some decrease in vascular tonus.

After reinfusion of blood the rheographic parameters reflecting the state of pulmonary circulation gradually returned to normal; nevertheless, even 2 h after reinfusion they were below base levels. Examination of circulation in the finger revealed peripheral hemodynamic changes, namely, reliable decrease ($P<0.05$) in pulsed delivery of blood with concurrent moderate increase in vascular tonus in the region in question. These changes were evaluated as a manifestation of deferred activation of the sympathetic branch of the central nervous system, which led to vasoconstriction and decreased blood flow in organs. Blood gas composition revealed decline of pCO_2, as compared to the prephlebotomy data, by a mean of 3.4 mm Hg ($P<0.05$). With regard to blood ABB, the subjects presented a decrease in SB ($P<0.05$), increase in BE ($P<0.05$) and tendency toward decline of blood pH. These findings were indicative of compensatory metabolic acidosis at this time, and it was apparently due to impairment of tissular homeostasis as a result of constriction of peripheral blood vessels.

These data indicate that even after submitting subjects to AOH, the pulmonary vessels serve as a reservoir during the time of reduction in circulating blood volume and probably enable us to interpret the increase in delivery of blood to the lungs during AOH as a reflex mechanism of pooling blood by the body, perhaps in order to use it in the event of critical situations related to altered hemodynamics.

Retention and, in some cases, development of disturbances referable to regional hemodynamics and gas exchange after complete restitution of circulating blood volume is a reflection of the complicated reactions to moderate loss of blood after AOH. In such cases, reinfusion of more blood than was removed should be considered adequate.

BIBLIOGRAPHY

1. Kassil', V. L. and Ryabova, N. M., "Iskusstvennaya ventilyatsiya legkikh v reanimatologii" [Artificial Ventilation of the Lungs in Resuscitation Practice], Moscow, 1977.

2. Oberg, B., in "International Symposium on Control of Vascular Capacity. Transactions," Moscow, 1977, pp 109-120.

3. Shershnev, V. G., Dzyak, G. V. and German, A. K., in "Klinicheskaya reografiya" [Clinical Rheography], Kiev, 1977, pp 19-86.

4. Yarullin, Kh. Kh., Krupina, T. N., Vasil'yeva, T. D. et al., KOSMICHESKAYA BIOL., No 4, 1972, pp 33-39.

5. Aarseth, P., ACTA PHYSIOL. SCAND., Vol 83, 1971, pp 60-69.

6. Astrup, P., Jorgensen, K., Andersen, O. S. et al., LANCET, Vol 1, 1960, pp 1035-1039.

7. Tindall, G. T., Robinson, S. C., Grimson, B. et al., SURGERY, Vol 61, 1967, pp 248-255.

UDC: 616.36-008.939.15-02:612.766.2

ACTIVATION OF LIPID PEROXIDATION IN THE LIVER UNDER HYPOKINETIC CONDITIONS AND ITS PREVENTION WITH ANTIOXIDANTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 14 Oct 83) pp 48-52

[Article by Ye. N. Panasyuk, and L. N. Skakun]

[English abstract from source] Experiments on white rats showed that exposure to hypokinesia increased peroxidation of unsaturated fatty acids of lipids of cell membranes, decreased the content of sulfhydryl groups, and increased the content of disulphide groups. This was very marked during the first 4-7 days, i.e., during the time of a distinct stress-reaction. At later stages the rate of free radical processes decreased slightly. In the recovery period that followed 7-day hypokinesia lipid peroxidation in the rats gradually returned to normal. The initiation of free radical reactions during hypokinesia can be prevented by means of antioxidants (acetate tocopherol, sodium selenite) and syrepar.

[Text] The investigations of a number of authors established that, under hypokinetic conditions, particularly in the first hours and days of exposure to hypokinesia, a drastic gradient of afferent muscular impulsation leads to stress, which is effected through the hypothalamo-hypophyseo-adrenal system [10, 17, 21]. This is associated with increase in ACTH content of the pituitary, increase in mass and function of the adrenals [1, 9, 16, 22, 23], reduction in mass of the thymus and spleen, as well as in number of lymphocytes in lymphatic organs, decrease in absolute blood eosinophil count; however, there is increase in number of macrophage elements [19].

Functional impairment of the digestive system [6, 25, 27], appearance of gastric and duodenal ulcers [29-31, 33] are important manifestations of stress during hypokinesia. In such a situation, the high activity of physiological systems is not supported by the required energy of metabolism. There is depletion of the antioxidant system and change of oxidation of substrates, including cell membrane lipids, to the free-radical pathway [5, 14]. This is indicated by the increase in levels of free radicals in red blood cells [12], decrease in their resistance to acid hemolysis [7], faster development of peroxide atherosclerosis and arteriosclerosis [3].

Intensification of lipid peroxidation (LPO) during hypokinesia and in the post-hypokinetic recovery period is associated with poorer replenishment of the NADP·H and NAD·H pool [4]. Evidently, decline of liver phospholipid content [18], which is an important element of the body's antioxidant system [8], is instrumental in initiating LPO during hypokinesia.

We investigated peroxidation of unsaturated fatty acids of lipids of hepatic cell membranes during hypokinesia and the recovery period, as well as the effect on this process of agents with antioxidant properties.

Methods

Experiments were performed on 94 mongrel white male rats weighing 140-170 g. The animals were kept at the usual vivarium temperature (25-28°C) and ambient humidity on a standard diet. The model of hypokinesia was produced by placing the animals in special box-cages.

We assessed LPO according to levels of diene conjugates and malonic dialdehyde in blood and liver homogenates [15]. After decapitating the animals, blood was collected in chemically clean tubes treated with heparin. Pieces of liver free of blood and cooled were ground in a Downs type glass homogenizer. We used 10% homogenates for analysis. Their optical density was measured on an SF-16 spectrophotometer at a wavelength of 233 nm for the diene conjugates and 532 nm for malonic dialdehyde. We calculated the amounts of these LPO products by means of coefficients of molar extinction, $2.2 \cdot 10^5$ $mol^{-1}cm^{-1}$ for diene conjugates and $1.56 \cdot 10^5$ $mol^{-1}cm^{-1}$ for malonic dialdehyde.

We also assayed in whole blood and supernatant fraction of liver homogenates the sulfhydryl (SH) and disulfide (-S-S) groups of water-soluble proteins and low molecular compounds by the spectrophotometric method based on change in increment of optical density in the range of 250-255 nm, which occurs when p-mercuribenzoate is joined with SH groups [20]. Recrystallized and freshly prepared saturated sodium sulfide solution [26] and 8 M urea solution [24] were used to reduce -S-S bonds. The number of SH groups was determined by the standard curve plotted with glutathione and expressed in millimols per liter whole blood and in micromoles per gram wet liver tissue.

Results and Discussion

According to the data listed in Table 1, during hypokinesia there is impairment of intensity of peroxidation of unsaturated fatty acids of hepatic cell membrane lipids. This is confirmed by the increase in diene conjugates and malonic dialdehyde in liver homogenates and blood. As early as the 4th day of restricted mobility there is significant increase in diene conjugate content of the liver (on the average from 0.810±0.080 to 1.580±0.170 μmol/g organ, or almost 2-fold). On the 7th day of hypokinesia, the levels of these LPO products remained high in the liver and rose in blood (on the average from 76.14±8.11 to 112.58±5.76 μmol/ℓ, or 1.5-fold increase). In addition there was an increase in malonic dialdehyde content of liver homogenates (from 87.18±4.39 to 105.77±2.75 nmol/g). Thereafter, on the 15th day, the levels of these products dropped in blood but remained high in the liver. On the 30th day they were elevated both in blood and the liver.

Table 1. Effect of long-term hypokinesia on lipid peroxidation, SH and disulfide group content in liver and blood of white rats (M±m)

Biochemical parameter	Control	Day of hypokinesia			
		4	7	15	30
LPO products in blood: malonic dialdehyde, μmol/ℓ	6,94±0,38	5,88±0,42	7,37±0,55	4,92±0,65*	9,30±0,36*
diene conjugates, μmol/ℓ	76,14±8,11	52,00±5,39*	112,58±5,76*	75,00±4,50	102,27±5,05*
LPO products in the liver: malonic dialdehyde, nmol/g	87,18±4,39	95,08±5,08	105,77±2,75*	105,12±5,73*	123,93±8,05*
diene conjugates, μmol/g	0,810±0,080	1,580±0,170*	1,530±0,120*	0,980±0,140*	0,960±0,060
SH groups in blood, μmol/ℓ	20,92±1,55	17,35±0,72*	18,60±0,78	22,85±0,95	23,04±0,35
-S-S groups in blood, μmol/ℓ	2,21±0,20	3,50±0,69*	2,85±0,21	2,30±0,27	1,92±0,13
SH groups in liver, μmol/g	18,83±0,59	12,08±0,21*	11,98±0,46*	17,54±1,06	18,53±0,39
-S-S groups in liver, μmol/g	2,30±0,30	3,74±0,35*	4,03±0,28*	3,26±0,42*	2,83±0,10

* $P < 0,05$ as compared to control.

Consequently, during hypokinesia there is intensification of free-radical oxidation of unsaturated fatty acids of liver lipids, particularly on the first 4-7 days, i.e., during the period of marked stress reaction. Thereafter, the intensity of the process diminishes somewhat.

Concurrently, during hypokinesia there is change in sulfhydryl and disulfide group content of protein and low molecular substances in the liver and blood (see Table 1). In particular, there was decline of SH group level, but rise of disulfide group level, particularly on the 4th and 7th days of hypokinesia. Thus, the quantity of SH groups in liver homogenates was 36% lower on the 4th day and 36.5% lower on the 7th day than in the control. At the same time, disulfide group content of the liver exceeded by more than 1.5 times the control level. In blood, the deficit of SH groups constituted 17.1% on the 4th day, and there was significant increase in disulfide groups. On subsequent days there was equalization of parameters of SH and -S-S group content in both the liver and blood.

The above-described changes are indicative of significant disturbances in redox processes in the body under hypokinetic conditions. Most changes were

observed on the first days of restricted motor activity of animals, i.e., during the period of a marked stress state when there is the greatest intensification of free-radical reactions.

In the recovery period following hypokinesia there is gradual normalization of free-radical oxidation of hepatocyte lipids within 7 days. Already on the 3d day, diene conjugate content decreased on the average from 1.530±0.120 to 1.140±0.060 μmol/g, or by 34.2% (Table 2), while the level of malonic aldehyde in liver homogenates not only failed to decline, but even rose by an average of 16.3%. Nevertheless, by the 7th day of the recovery period there was a decrease in amount of this LPO product to 103.60±8.27 nmol/g and of diene conjugates to 0.960±0.07 μmol/g. There was no complete restoration of LPO, but there was a significant shift in the direction of normalization.

Table 2.
Effect of posthypokinetic recovery on peroxidation of lipids in white rat liver (M±m)

Series of experiments	LPO products in liver	
	malonic dialdehyde, nmol/g	diene conjugates, μmol/g
I Control	87,18±4,39	0,810±0,080
II Hypokinesia, 7th day	105,77±2,75	1,530±0,120
P_{I-II}	<0,01	<0,001
III Recovery, 3d day	123,00±8,27	1,140±0,060
P_{I-III}	<0,01	<0,01
P_{II-III}	>0,05	<0,02
IV Recovery, 7th day	103,60±8,27	0,960±0,070
P_{I-IV}	>0,1	>0,1
P_{II-IV}	>0,5	<0,01

Note: Here and in Table 3, 6 experiments were performed in each series.

Table 3.
Effect of syrepar, tocopherol acetate and sodium selenite on lipid peroxidadation in liver of hypokinetic white rats (M±m)

Series of experiments	LPO products in liver	
	malonic dialdehyde, nmol/g	diene conjugates. μmol/g
I control	96,14±4,96	0,882±0,065
Hypokinesia, 4th day:		
II background	111,70±11,58	1,248±0,114
III syrepar	86,76±7,03	0,636±0,053
P_{II-III}	0,1	<0,001
IV tocopherol acetate	100,86±9,10	0,828±0,073
P_{II-IV}	>0,25	<0,02
V Sodium selenite	92,30±5,79	0,855±0,050
P_{II-V}	>0,1	<0,01
VI tocopherol acetate + Na selenite	97,44±7,45	0,903±0,061
P_{II-VI}	0,25	<0,05

It is possible to prevent LPO impairment in the liver under hypokinetic conditions by means of drugs with antioxidant action, in particular, tocopherol acetate, sodium selenite and syrepar were used. This is shown by the data in Table 3. Rats kept under hypokinetic conditions for 4 days were given syrepar (subcutaneously, 0.1 mℓ/0.1 kg weight), tocopherol acetate (intramuscularly, 5 mg/0.1 kg) and sodium selenite (subcutaneously, 3 μg/0.1 kg) or a combination of tocopherol acetate and sodium selenite (in the same doses) daily. It was found that all of these agents prevented initiation of LPO in the liver by hypokinesia to about the same extent. They eliminated entirely activation of

this process in the liver. Thus, syrepar had antioxidant properties. Under its effect, malonic dialdehyde content of hepatic homogenates held at the base level, while there was half as much diene conjugates than in rats submitted to hypokinesia without this agent and 28% less than in control animals. Evidently, syrepar contains substants that are mandatory constituents of the liver's antioxidant system. They could be phospholipids, low molecular substances containing SH groups, tocopherols, etc.

Demonstration of antioxidant properties in syrepar means that there is a possibility of expanding its use in medical practice, in particular, for prevention and treatment of diseases, in the pathogenesis of which initiation of free-radical reactions of lipid oxidation plays an important part.

Apparently, intensification of free-radical reactions, including LPO, plays an important role in certain morphological, ultrastructural and functional disturbances that develop in the liver, myocardium, skeletal muscles and other organs during hypokinesia. It is known that free radicals and LPO products, especially hydroperoxides, are highly toxic. They impair cell division and growth, elicit swelling, adhesion and even dissociation of mitochondria, they inactivate thiol enzymes involved in respiration, glycolysis and other processes, they separate tissue respiration and oxidative phosphorylation [28, 32]. By enhancing protein breakdown, they are instrumental in release of tissue toxins (histamine, choline, quinones) and elicit fatty dystrophy of parenchymatous organs, particularly the liver. Under the influence of these products there is reduction of body weight and impairment of visceral functions [8, 11]. Of the internal organs, the liver is notable for highest sensitivity to LPO products [2, 15]. For this reason, activation of LPO should be viewed as an important (if not deciding) element in the pathogenesis of stressor damage to the liver. Such a conception had been advanced previously with regard to the role of LPO in stress-produced damage to the myocardium [13].

BIBLIOGRAPHY

1. Vinogradov, V. N., Petrukhin, V. G. and Fedorov, I. V., BYULL. EKSPER. BIOL., No 6, 1968, pp 96-99.

2. Vladimirov, Yu. A. and Archakov, A. I., "Perekisnoye okisleniye lipidov v biologicheskikh membranakh" [Lipid Peroxidation in Biological Membranes], Moscow, 1972.

3. Voskresenskiy, O. N., Devyatkina, T. A., Bezuglyy, Yu. V. et al., in "Aktual'nyye voprosy farmakologii i toksikologii" [Pressing Problems of Pharmacology and Toxicology], Ternopol, 1981, pp 27-28.

4. Voskresenskiy, O. N., in "Adaptatsiya i adaptogeny" [Adaptation and Adaptogens], Vladivostok, 1977, pp 91-96.

5. Voskresenskiy, O. N., Zhutayev, I. A., Bobyrev, V. N. et al., VOPR. MED. KHIMII, No 1, 1982, pp 14-27.

6. Goland-Ruvinova, L. G., Vinogradov, V. A. and Goncharova, N. P., KOSMICHESKAYA BIOL., No 1, 1983, pp 30-33.

7. Golotin, V. G., Gonenko, V. A. and Dobryakova, A. I., in "Fiziologicheskiye i klinicheskiye problemy adaptatsii cheloveka i zhivotnogo k gipotermii, gipoksii i gipodinamii" [Physiological and Clinical Problems of Human and Animal Adaptation to Hypothermia, Hypoxia and Hypodynamia], Moscow, 1975, pp 153-154.

8. Zhuravlev, A. I. and Zhuravleva, A. I., "Sverkhslaboye svecheniye syvorotki krovi i yego znacheniye v kompleksnoy diagnostike" [Extremely Weak Fluorescence of Blood Serum and Its Significance to Comprehensive Diagnostication], Moscow, 1975.

9. Kirichek, L. T., Zholudeva, V. I. and Kharchenko, N. S., in "Farmakologiya i toksikologiya" [Pharmacology and Toxicology], Kiev, Vyp 16, 1981, pp 39-41.

10. Kovalenko, Ye. A. and Gurovskiy, N. N., "Gipokineziya" [Hypokinesia], Moscow, 1980.

11. Kudryashov, Yu. B., "Some Properties and Nature of Hemolytic Factor Appearing in Animal Liver in the Presence of Radiation Sickness," author abstract of candidatorial dissertation, Moscow, 1966.

12. Manik, A. P., in "Adaptatsionnyye problemy kosmicheskoy biologii i meditsiny" [Adaptation Problems of Space Biology and Medicine], Moscow, 1980, pp 42-43.

13. Meyerson, F. Z., Golubeva, L. Yu., Kagan, V. Ye. et al., in "Metabolizm miokarda" [Myocardial Metabolism], Moscow, 1981, pp 237-251.

14. Meyerson, F. Z., Kagan, V. Ye., Prilipko, L. L. et al., BYULL. EKSPER. BIOL., No 10, 1979, pp 404-406.

15. Platser, Z., Vidlakova, M. and Kuzhela, L., CHEKHOSL. MED. OBOZR., Vol 16, No 1, 1970, pp 30-41.

16. Portugalov, V. V., Gazenko, O. G., Il'ina-Kakuyeva, Ye. A. et al., KOSMICHESKAYA BIOL., No 6, 1967, pp 18-25.

17. Potapov, A. N., Ibid, No 2, 1972, pp 16-20.

18. Ryl'nikov, Yu. P., Ibid, No 2, 1974, pp 8-13.

19. Tikhonova, G. P. and Bizin, Yu. G., Ibid, No 5, pp 27-30.

20. Torchinskiy, Yu. M., "Sera v belkakh" [Sulfur in Proteins], Moscow, 1977, p 118.

21. Fedorov, I. V., KOSMICHESKAYA BIOL., No 4, 1971, pp 59-61.

22. Fedorov, I. V. and Grishanina, L. A., Ibid, No 3, 1967, pp 43-48.

23. Yurgens, I. L. and Kirillov, O. I., Ibid, No 4, 1972, pp 3-6.

24. Anfinsen, C. B. and Haber, E., J. BIOL. CHEM., Vol 236, 1961, pp 1361-1365.

25. Arosa, P., Bordeianu, A., Cananau, S. et al., REV. ROUM. MORPH., Vol 15, 1978, pp 249-251.

26. Clarke, H. T., J. BIOL. CHEM., Vol 97, 1932, pp 235-240.

27. Deysine, M., Katzka, D. and Rosario, E., AM. J. GASTROENT., Vol 67, 1977, pp 152-156.

28. Hjelle, J. J., Grubbs, J. and Petersen, D. R., TOXICOL. LETT., Vol 14, 1982, pp 35-43.

29. Kasper, H., Brodersen, M. and Schedel, K., ACTA HEPATO-GASTROENT. (Stuttgart), Vol 22, 1975, pp 403-408.

30. Neumann, G. and Petzold, H., Z. GES. INN. MED., Vol 21, 1977, pp 581-583.

31. Schwille, P. O., Schellerer, W. and Samburger, N. M., BULL. SOC. INT. CHIR., Vol 34, 1975, p 245.

32. Trush, M. A., Mimnaugh, E. G. and Gram, T. E., BIOCHEM. PHARMACOL., Vol 32, 1982, pp 3335-3346.

33. Zierden, E., Henyst, K., Wayner, H. et al., RES. EXP. MED., Vol 168, 1976, pp 199-201.

UDC: 616.127-018.1-02:[612.766.2+612.014.481/.482

SPECIFICITY OF ULTRASTRUCTURAL CHANGES IN RAT MYOCARDIUM SUBMITTED TO HYPOKINESIA AND RADIATION DAMAGE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 13 May 83) pp 53-55

[Article by V. S. Romanov and L. A. Bespalova]

[English abstract from source] By electron microscopy and morphometry cardiomyocytes of 20 rats gamma-irradiated with a single dose of 180.6 μCi/kg and those of 20 rats exposed to hypokinesia for 10 days were examined. Visually the ultrastructural changes of cardiomyocytes were nonspecific. The morphometric examination revealed specific features of ultrastructural rearrangements in the nuclei and mitochondria of cardiomyocytes of rats on day 10 of hypokinesia and irradiation.

[Text] In the opinion of some researchers [1, 4-6, 9], various types of accelerations, radiation, as well as hypokinesia, which are present during long-term spaceflights, elicit qualitatively similar ultrastructural changes in the myocardium of animals, and they are nonspecific. New approaches are needed for additional evaluation of submicroscopic structures of myocardial cells, which could help determine the specificity of the observed changes to each type of factor individually.

As such a method, we have used here morphometric electron microscopy of animals' cardiomyocytes with exposure to hypokinesia and radiation.

Methods

Male rats weighing 200±10 g were divided into three groups: the 1st group consisted of 20 intact rats serving as a control; the 2d, 20 rats tested under hypokinetic conditions, which were produced by placing the animals in special box-cages that restricted motor activity; the animals of the 3d group (20 rats) were exposed to a single dose of radiation, 180.6 mC/kg delivered by an EGO-2 unit. Experimental and control rats were in the same room and on the same diet. Animals were decapitated on the 10th day after exposure, as this experimental time was considered the beginning of "true" hypokinesia [6, 9] and the "height" of radiation sickness [4]. The heart was rapidly removed from the thoracic cavity and cooled on ice until heart beats stopped. Then, identical segments of the middle of the left ventricle were placed in

2.5% glutaraldehyde solution (pH 7.4). The material was then fixed in osmium tetroxide according to Millonig and, after standard dehydration, the specimens were imbedded in a mixture of epon and araldite. An LKB-4800A microtome was used to prepare ultrafine sections, they were contrasted with lead citrate [12] and viewed under a JEM-100B electron microscope. Morphometric data were obtained with use of stereological principles of cytology [11]. Stereological analysis was made on cross sections with test grids at 15,000× magnification. On the electronograms, we determined the share of euchromatin area in relation to total area of the nucleus (S_e/S_n) expressed as a percentage, the number of mitochondria per unit cardiomyocyte area (n_{mc}), relative area of each organelle (S_{mc}) and total area of mitochondria (ΣS_{mc}).

Statistical processing was performed according to Student.

Results and Discussion

On the 10th day of hypokinesia, the rats' weight was 17% less than in the control ($P<0.01$), absolute heart mass decreased by 3% ($P<0.02$), the weight of irradiated animals was in the range of statistical error and constituted 196±10 g. Thus, 10-day hypokinesia elicited more marked changes in rats than single exposure to γ-radiation in a dosage of 180 mC/kg [millicoulomb/kg].

Electron microscopy of cardiomyocytes of rats submitted to hypokinesia and exposed to radiation revealed nonspecific changes in the nucleus, mitochondria, sarcoplasmic reticulum (SPR) and myofibrils.

On the 10th day after hypokinesia, cardiomyocyte nuclei presented clearing of karyoplasm, invagination of the nuclear membrane and condensation of heterochromatin along it, nuclear pores and SPR elements were dilated. All this is indicative of intensification of nuclear-sarcoplasmic transport and activation of the protein-synthesizing system of cardiomyocytes [6, 9]. After exposure to radiation, nuclear pores were virtually undemonstrable, while heterochromatin on sections of cardiomyocyte nuclei occupied more of the nucleus than with hypokinesia. Not infrequently, there was dilatation of the perinuclear space with formation of lacunae due to protrusion of the external nuclear membrane. It is known that nuclear pyknosis is always associated with a decrease in DNA content [9]. After total-body exposure to γ-radiation, the size of the canals and SPR cisternae in cardiomyocytes was diminished, as was the number of ribosomes, which could be indicative of inhibition of nuclear-sarcoplasmic transport and depression of protein-synthesizing function of cells [1, 4].

Along with structural disturbances in the protein-synthesizing system of cardiomyocytes, we demonstrated changes in organelles responsible for energy metabolism in these cells. Thus, with the factors used, there was uneven change in mitochondria, not only in different cardiomyocytes, but in the same cell. The organelles were swollen, with an osmiophobic matrix, in which myelinoid structures were seen; the cristae showed change in topography and packing density. This is indicative of hyperfunction of organelles, which occurs due to damage to myocardial capillaries with exposure to hypokinesia and γ-radiation [1, 7, 9]. The changes in ultrastructure of the contractile system of cardiomyocytes were manifested by formation of local contractures and lysis of myofibrils. These findings are indicative of marked structural

reorganization of cardiomyocyte organelles after the experiments. It must be noted that such submicroscopic changes had been demonstrated in the myocardium in the presence of hypoxia, hypothermia and accelerations [1-3, 5-8].

Thus, on the basis of comparative analysis of electron microscope findings it can be concluded that the ultrastructural changes in rat cardiomyocytes, which develop 100 days after exposure to ^{60}Co γ-radiation in a dosage of 180.6 mC/kg, as well as under hypokinetic conditions, have the same type of nonspecific features. Unfortunately, there are virtually no data in the literature about morphometric analysis of ultrastructural changes in organelles during development of nonspecific reactions to different factors, including hypokinesia and γ-radiation.

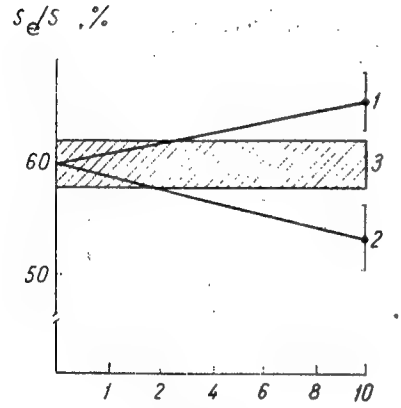


Figure 1. Redistribution of chromatin in rat cardiomyocyte nuclei after exposure to γ-radiation in a dose of 180.6 mC/kg and hypokinesia
X-axis, postexposure days;
y-axis, share of euchromatin area (S_e) in relation to total area of nucleus (S_n)(%). Here and in Figure 2:
1) hypokinesia 3) control
2) γ-radiation

The results of our stereological analysis revealed (Figure 1) that the share of euchromatin in cardiomyocyte nuclei increases by 6% by the 10th day of hypokinesia, whereas it decreases by 7% after γ-irradiation ($P<0.03$). This state of chromatin is consistent with the low level of metabolic activity of this type of nuclei [9]. Thus, we succeeded in confirming with the morphometric method the validity of electron microscopic data concerning depression of metabolism of cardiomyocyte metabolism following exposure to γ-radiation and its activation following hypokinesia.

Estimation of mitochondria per unit cardiomyocyte area revealed that their number was 1.4-fold increased on the 10th day of hypokinesia ($P<0.03$). This parameter did not differ reliably from the control level after exposure to γ-radiation (Figure 2a).

As shown by morphometric analysis (Figure 2b), the increase in number of mitochondria per unit cardiomyocyte area on the 10th day of hypokinesia was associated with 2.6-fold reduction in their "size," as compared to the control level ($P<0.04$). After exposure to γ-radiation, the mitochondrial "size" index was 1.6 times higher than the control level ($P<0.02$), as can be seen in Figure 2b. Ten days after the experiments there was statistically reliable increase in the indicator of total area of rat cardiomyocyte mitochondria with use of the indicated extreme factors (Figure 2c). The index of total mitochondrial area rose by 15%, as compared to the control, after exposure to radiation and by 23% after hypokinesia ($P<0.03$). As shown by morphometric analysis, the increase in total mitochondrial area after exposing rats to γ-radiation in a dosage of 180.6 mC/kg occurred due to increase in area of each organelle, their number remaining constant, whereas after hypokinesia it occurred due to drastic increase in number of mitochondria with concurrent reduction of

organelle area. Thus, it can be assumed that the increase in area of each cardiomyocyte mitochondrion after exposure to radiation is due to its swelling [1, 4, 7], while the reduction of organelle area after hypokinesia is due to their division or de novo production [5, 6, 9]. Such ultrastructural changes in rat cardiomyocyte organelles had been demonstrated by us previously following local exposure to the animals' heart to γ-radiation [10]. However, as shown by morphometric analysis, all of the tested parameters of rat cardiomyocytes were considerably higher following total-body γ-irradiation in a dosage of 180.6 mC/kg than after local irradiation of the region of the heart in a dosage of 516 mC/kg.

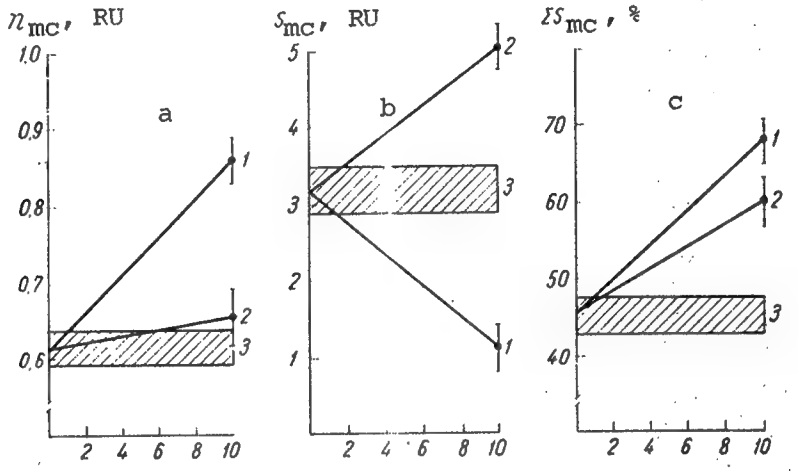


Figure 2. Changes in number, area and total area of rat cardiomyocyte mitochondria after hypokinesia and exposure to γ-radiation.
X-axis, postexposure days; y-axis:
a) number of mitochondria per unit cardiomyocyte area (relative units--RU)
b) average area of one mitochondrion (RU)
c) total mitochondrial area (%)

Consequently, on the basis of morphological analysis of ultrastructural changes in rat cardiomyocyte organelles following acute radiation damage with ^{60}Co in a dosage of 180.6 mC/kg and 10-day hypokinesia, it can be concluded that the developing changes are nonspecific, which is indicative of compensatory-adaptive reactions of rats to these factors. However, as shown by morphometric analysis, the mechanism of reorganization, in particular, in nuclei and the mitochondrial system, under the effect of these extreme factors is referable to different routes: "enlargement" of mitochondria in the case of radiation and due to accelerated de novo formation in the case of hypokinesia.

Thus, the method of morphometric evaluation of ultrastructural changes in rat cardiomyocytes, which we selected, made it possible to demonstrate the mechanism of compensatory-adaptive reactions and to establish the specific nature of submicroscopic changes in nuclei and mitochondria on the 10th day of hypokinesia and radiation damage.

BIBLIOGRAPHY

1. Bespalova, L. A., KOSMICHESKAYA BIOL., No 3, 1973, pp 26-30.

2. Bespalova, L. A. and Romanov, V. S., in "O problemakh mikrotsirkulyatsii (funktsiya i struktura)" [Problems of Microcirculation (Function and Structure], Moscow, 1977, pp 13-14.

3. Yeriskovskaya, N. K. and Tsellarius, Yu. G., BYULL. EKSPER. BIOL., No 11, 1976, pp 1380-1382.

4. Ivanov, A. Ye., Kurshakova, N. N. and Shikhodyrov, V. V., "Patologicheskaya anatomiya luchevoy bolezni" [Pathological Anatomy of Radiation Sickness], Moscow, 1981.

5. Katunyan, P. I. and Romanov, V. S., KOSMICHESKAYA BIOL., No 3, 1981, pp 82-83.

6. Kovalenko, Ye. A. and Gurovskiy, N. N., "Gipokineziya" [Hypokinesia], Moscow, 1980.

7. Manteyfel', V. M., IZV. AN SSSR. SER. BIOL., No 2, 1971, pp 38-47.

8. Nepomnyashchikh, L. M. and Kolesnikova, N. A., Ibid, No 8, 1977, pp 247-250.

9. Romanov, V. S., "Effect of Long-Term Hypokinesia on the Rat Myocardium (Electron-Microscope Study)," author abstract of candidatorial dissertation, Moscow, 1977.

10. Romanov, V. S. and Bespalova, L. A., RADIOBIOLOGIYA, No 2, 1981, pp 238-242.

11. Tashke, K., "Vvedeniye v kolichestvennuyu tsitogistologicheskuyu morfologiyu" [Introduction to Quantitative Cytohistological Morphology], Bucharest, 1980.

12. Reynolds, G. S., J. CELL BIOL., Vol 17, 1963, pp 208-212.

UDC: 617.741-004.1-092.9-02:615.849.114

LENTICULAR OPACITIES IN MICE EXPOSED TO HELIUM IONS WITH ENERGY OF 4 GeV/NUCLEON AND ^{60}Co GAMMA RADIATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, Jan-Feb 85 (manuscript received 2 Dec 83) pp 56-58

[Article by A. N. Kabachenko and B. S. Fedorenko]

[English abstract from source] The cataractogenic effect of helium ions with the energy 4 GeV/nuclon and ^{60}Co gamma-radiation was examined. In response to helium irradiation the cataract incidence and maturation rate was higher than in response to gamma-irradiation at the same doses. The RBE coefficients of helium ions were calculated from the equally effective doses of reference and helium irradiations. They depended on the exposure duration and amounted to 1.2±0.1, 2.2±0.1 and 2.6±0.1 by post-irradiation weeks 20, 30, and 40, respectively.

[Text] Studies of biological effects of heavy nuclei of galactic cosmic radiation (GCR), which were conducted on the most elementary biological objects and plants [2, 5], warrant the belief that passage of such particles through cells with low repair capacity could present a danger to them. For this reason, it was deemed important to investigate the biological effects of accelerated high-energy helium ions contained in GCR on the lens of the mouse eye, and to determine the coefficients of relative biological effectiveness (RBE) of this type of radiation.

Methods

In our experiments, we used 430 female F_1(CBA×C_{67}Bl) mice weighing 16-18 g. The animals were exposed to total-body radiation by helium ions with energy of 4 GeV/nucleon in doses of 0.5, 1.0, 2.0 and 4.0 Gy, and ^{60}Co γ-radiation delivered by an RKh-γ-3 unit, in doses of 1.0, 2.0, 4.0 and 6.0 Gy. Radiation dose rate constituted 0.002 and 0.006 Gy/s for helium and γ-radiation, respectively. LET [linear energy transfer] constituted 8.8 MeV•cm^2/g for helium ions and 2.5 MeV•cm^2/g for γ-radiation. The animals were irradiated on the synchrophasotron of the Joint Institute for Nuclear Research in Dubna. The lenses of irradiated and control animals were examined every 4 weeks with an electro-ophthalmoscope and +15.0 D magnifying glass. The pupils were dilated with 1% homatropine solution. In defining degree of opacity, we distinguished

four stages: I--formation of individual punctate opacities; II--point opacities that merged forming a small opaque disk; III--the disk increases in size giving off rays toward the periphery and it is difficult to see the fundus; IV--complete opacity of lens [3]. The incidence of lenticular opacities was calculated as percentage of examined eyes in each group of animals. The obtained data were processed statistically by the χ^2 method.

Results and Discussion

The results of these studies revealed that mice exposed to high-energy helium ions in doses of 0.5 to 4.0 Gy develop lenticular opacities just as they do after exposure to γ-radiation in doses of 1.0-6.0 Gy. However, the time of appearance of visible changes in the lens differed. After exposure of animals to helium ions in a dose of 4.0 Gy, the first punctate lenticular opacities were detected 4 weeks later, and with doses of 1.0 and 2.0 Gy 8 weeks after exposure. In mice exposed to γ-radiation in doses of 4.0 and 6.0 Gy, the first opacities appeared 8 weeks after exposure, and with doses of 1.0 and 2.0 Gy, 10 weeks after exposure. Figure 1 illustrates duration of latency period as a function of radiation dose. In nonirradiated animals, the first senile opacities of the lens appeared only 20 weeks after the start of the experiment.

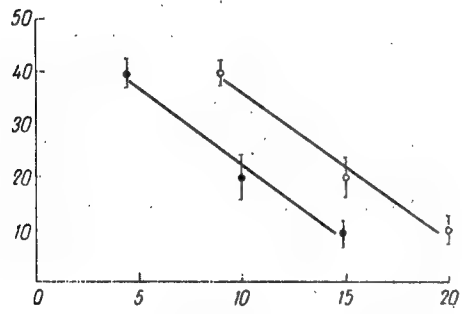


Figure 1.
Duration of latency period of formation of lenticular opacities as a function of dose of helium ions (dots) and γ-radiation (circles)

The incidence of lenticular opacities increased in irradiated animals with increase in dosage. Analysis of the results revealed that, in the case of helium ions, the incidence of lenticular opacities as a function of dose was linear in the dose range of 0.5 to 2.0 Gy. Thereafter, the curve of this function forms a plateau (Figure 2a). In the indicated range of doses, the dose-effect curve can be described by a linear equation.

With exposure to γ-radiation, the dose-effect curve had a somewhat different appearance. It was linear (Figure 2b) in the dose range of 1.0 to 4.0 Gy. The value of coefficient α changed from 14.6 by the 20th week after irradiation to 19.5 by the 30th week. In this case, the slope of the curve was less marked by one-half than with exposure to helium. This is indicative of the higher intensity of formation of lenticular opacities with exposure to helium ions.

The values for RBE of helium ions with energy of 4 GeV/nucleon (opacities in 50% of the cases) were different for the 20th, 30th and 40th postradiation weeks, and they constituted 1.2±0.1, 2.2±0.1 and 2.6±0.1, respectively.

A variation of values for the RBE coefficient as a function of time of examination of incidence of opacities was also found when rabbits were exposed to accelerated argon ions (LET = 90 keV/μm) and neon (LET = 35 keV/μm) [4]. High doses of radiation led to lenticular opacity before complete loss of

vision, whereas with low doses there was development of only partial (incomplete) cataract. The rate of cataractogenesis increased with increase in radiation LET. It should also be noted that in experiments on different biological objects, according to cytogenetic parameters RBE coefficients for helium ions with energy of 4.6 GeV/nucleon were in the range of 1.2-2.7 [1]. The high values for helium ion RBE are attributed by authors to the contribution of secondary radiation appearing as a result of nuclear interactions as charged particles pass through cells. There can be appearance of slower charged particles (protons, α-particles, etc.), the LET of which exceeds that of the original radiation.

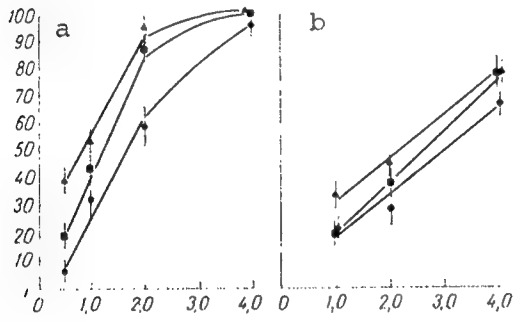


Figure 2.
Incidence of lenticular opacities as a function of dosage of helium ions (a) and γ-radiation (b) 20 (●), 30 (■) and 40 (▲) weeks after irradiation
X-axis, dose (Gy); y-axis, incidence of opacities (%)

Values of coefficient b for different doses of helium ions and γ-radiation*

Dosage, Gy	Helium ions (He)	γ-radiation (γ)	b (He)/b (γ)
1,0	1,83	1,46	1,25
2,0	3,25	1,55	2,09
4,0	5,20	2,12	2,45

*$N = a + bt$, where N is incidence of opacity (%), t is postradiation time (weeks), a is incidence of opacity in control animals and b is change in incidence of opacities in 1 week.

The incidence of development of opacities of the lens is a function of time elapsed since irradiation (Figure 3). The time-effect function is close to linear.

The data listed in the Table indicate that the intensity of formation of lenticular opacities is considerably greater after exposure to helium ions than γ-radiation, and in both instances it increases with increase in dosage.

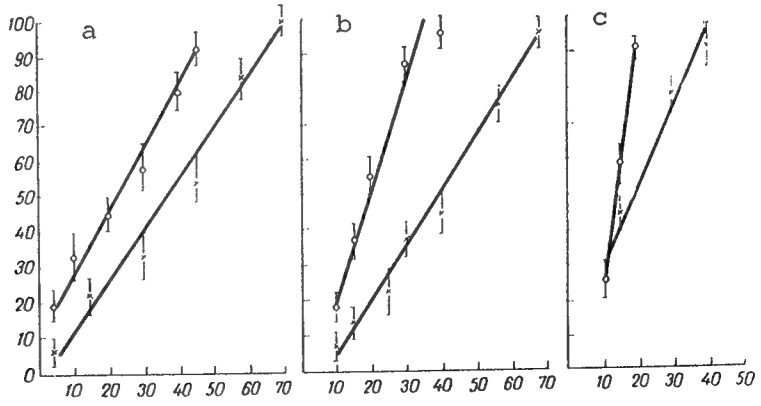


Figure 3. Incidence of lenticular opacities as a function of time after exposure to helium ions (○) and γ-radiation (×) in doses of 1.0 (a), 2.0 (b) and 4.0 (c) Gy.
X-axis, time of examination (weeks); y-axis, incidence of opacities (%)

The start of formation of punctate opacities classified as stage I of cataract development was observed at different times, depending on the radiation dose: 5-20 weeks after exposure to helium ions in doses of 4.0-0.5 Gy and 8-10 weeks after exposure to γ-radiation in doses of 4.0-1.0 (2.0) Gy. With increase in duration of the study the incidence of stage I opacities increased, reaching a maximum (75%) by the 20th week after exposure to 4.0 Gy helium ions. With exposure to radiation in doses of 2.0, 1.0 and 0.5 Gy, maximum number of stage I opacities was observed after 40, 50 and 70 weeks, respectively. Thereafter, the incidence of stage I opacities dropped due to start of formation of stage II cataract.

Development of stage II cataract was observed in some animals 15, 20, 30 and 39 weeks after delivery of 4.0, 2.0, 1.0 and 0.5 Gy helium ions, respectively. Progressive development of stage II opacities of the lens was noted only in animals exposed to doses of 1.0-4.0 Gy. With delivery of 0.5 Gy, stage II cataract was demonstrated in only 13% of the cases.

Stage III cataracts, which are characterized by almost complete opacity of the lens, were found in some animals exposed to helium ions in doses of 2.0 and 4.0 Gy by the 50th and 40th weeks, respectively. With increase in duration of the experiment, their frequency rose. In some animals of this group, there was development of complete cataract (stage IV) 77 weeks after irradiation.

There was analogous development of cataracts in animals exposed to γ-rays. In particular, formation of stage I opacities occurred less intensively, and the maximum did not exceed 40%. Stage II opacities appeared 5-10 weeks later than with exposure to helium ions. Development of stage III cataract was demonstrated in animals exposed to doses of 2.0 and 4.0 Gy also, but at a later time (55 weeks after exposure to a dosage of 4.0 Gy). With increase in postradiation time, their incidence also increased.

Thus, the results of our investigation revealed that 4 GeV/nucleon helium ions had a marked cataractogenic effect. The incidence of lenticular opacities was a function of radiation dosage and postradiation time. Formation of opacities is preceded by a latency period, the length of which diminishes with increase in dosage. The clinical signs of cataract development in mice exposed to helium ions did not differ from those associated with standard types of radiation. The coefficients of relative biological effectiveness of helium ions with energy of 4 GeV/nucleon changed as a function of tested time, and they constituted 1.2, 2.2 and 2.6 by the 20th, 30th and 40th weeks, respectively.

BIBLIOGRAPHY

1. Govorun, R. D., Vorozhtsova, S. V. and Gerasimenko, V. N., KOSMICHESKAYA BIOL., No 4, 1982, pp 64-67.

2. Nevzgodina, L. V. and Maksimova, Ye. N., Ibid, pp 67-71.

3. Christenberry, K. W. and Furth, J., PROC. SOC. EXP. BIOL. (New York), Vol 77, 1951, p 559.

4. Keng, P. C., Lee, A. C., Cox, A. B. et al., INT. J. RADIAT. BIOL., Vol 41, 1982, pp 127-137.

5. Planel, H., Soleilhavoup, J. P., Blangult, J. et al., LIFE SCI. SPACE RES., Vol 12, 1974, pp 85-89.

UDC: 615.5-001.29:546.291

SKIN LESIONS AFTER EXPOSURE TO HIGH-ENERGY PROTONS AND HELIUM IONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 25 Jul 83) pp 59-62

[Article by N. Ya. Savchenko]

[English abstract from source] The RBE of high-energy protons and helium ions was measured with respect to the proliferation rate, cell number of the epidermic basal layer, induction rate of aberrant mitoses, number and type of chromosome aberrations. The animals were examined on postradiation days 1 and 6 (i.e., when the proliferation rate of the first postradiation mitosis was at a maximum). The RBE coefficients of protons and helium ions were unity with respect to the reproductive cell death and cell number of the epidermic basal layer; 1.5 with respect to the formation of multiple cell aberrations; 1.2-1.5 with respect to exchange-type aberrations; and 1.6 with respect to the mitotic index variations. This gives evidence that in response to high-energy protons the nuclear apparatus of the cell undergoes profound lesions.

[Text] It is interesting to study the condition of the skin after exposure to high-energy heavy charged particles, which are the main component of radiation from solar flares as related to solving problems of assuring radiation safety of spaceflights [1].

Our objective here was to investigate the relative biological effectiveness (RBE) of protons and helium ions of relativistic energies according to cytological and cytogenetic criteria, which characterize the state of mouse skin at different postexposure stages.

Methods

In the experiments, we used 410 $F_1(CBA \times C_{57}Bl_6)$ mice of both sexes. The animals were irradiated on the synchrocyclotron of the Joint Institute for Nuclear Research in Dubna, to protons with energy of 9.2 GeV and helium ions with energy of 4 GeV/nucleon in doses of 0.05 to 7.5 Gy. Dose rate constituted 0.003-0.001 Gy/s, homogeneity of heavy particle beams was ±10%, with linear energy transfer (LET) of 0.2 and 0.88 keV/μm. The animals were examined 24 h after irradiation and at maximum parameters of proliferative activity of

the first postradiation mitosis [2]. We used 10-11 animals at each stage and for each dose of radiation. Concurrently, we fixed pieces of skin from mice in the intact group. Analogous dose-effect curves were studied on animals of the same line and weight exposed to ^{60}Co γ-quanta at a dose rate of 0.04 Gy/s. The following served as criteria of skin sensitivity to radiation: proliferative activity, cellularity of epidermal basal layer, incidence of induced aberrant mitoses, number of chromosome breaks per aberrant cell, incidence of appearance of cells with different types of chromosome aberrations. The material for cytological examination (pieces of mouse ear) was fixed in 10% neutral formalin, washed in tap water, placed in 1% acetic acid solution for 2-3 days, after which the epidermis (2 cell layers in thickness) was separated from the corium and cartilage by the method of Cowdry [3], washed thoroughly and stained with hematoxylin. After standard histological treatment, the material was placed in balsam and examined under a microscope. We counted the mean number of basal epidermal cells per standard microscope field, counting 50 such fields; we noted the number of dividing cells per 3000-5000; we counted aberrant cells per 50-100 cells at the late anaphase and early telophase. Cells with marked chromsome disturbances in the form of bridges and fragments were referred to aberrant mitoses [2]. The material was submitted to statistical processing using the least squares method and reliability criteria of Student [4].

Results and Discussion

The results of comparative study of the condition of mouse skin after exposure to heavy charged high-energy particles and ^{60}Co γ-quanta revealed the high inactivating activity of these types of radiation. There were disturbances of proliferative activity of epidermal cells and a high percentage of aberrant mitoses.

The damaging effect of radiation on the skin was characterized at the early stages by significant inhibition of mitotic activity of epidermal cells: 24 h after irradiation the number of dividing cells was at an extremely low level, with minimum values at high doses; the mitotic index did not exceed 20% of the control with a dosage of 1.0 Gy and 1.5% with 5.0 Gy. The degree of decline in capacity of epidermal cells for division can be characterized as:

$$\frac{M_c/N_c}{M_e/N_e} \cdot 100 = f(d)$$

Where M_e and M_c is the number of dividing cells in the experiment and control, N_e and N_c is the number of cells in the epidermal basal layer in the experiment and control, d is radiation dose (in Gy; Table 1). Analysis of the curves of change in mitotic index as a function of dosage 24 h after exposure shows that there were different effects of the tested types of radiation on proliferative activity of epidermal cells at different dose levels, and they were more distinct upon mathematical processing of the data. There was exponential decline of mitotic activity with doses up to 2.5 Gy, and it was characterized by proton and helium ion doses that lowered mitotic index by 50% and constituted 6.0±1.0 Gy. With increase in dosage to the median lethal level, the dose-effect curves acquired a more complicated appearance and were governed by a function that can be described satisfactorily with the polynomial formula:

$$y = a + bx + cx^2 + bx^3$$

where y is the mitotic index (% of control) and x is dose (Gy). Such a change in nature of the dose-effect curve at the early postradiation stages could be due to changes in proportion of cells at stages of the cell cycle differing in radiosensitivity and as a result of modification of more radioresistant processes. As we know, epidermal cells constitute an asynchronously dividing heterogeneous system of cell subpopulations at different levels of their functional and proliferative activity, which differ in radioresistance. With increase in radiation doses, at certain levels of damage, there may be involvement of previously resistant subpopulations in the process. The curves of degree of depression of mitotic activity as a function of dosage 24 h after exposure to different factors are qualitatively rather similar. However, calculation of RBE coefficients for protons and helium ions, which was made on the basis of comparing doses eliciting 50% decline of the mitotic index yielded values of 1.6±0.5 in both instances.

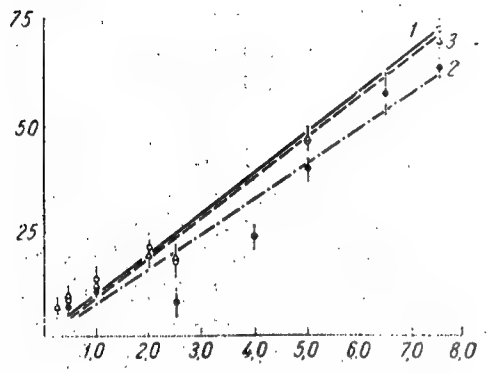
Table 1.
Changes in mitotic activity of epidermal cells 24 h after irradiation, and number of chromosome breaks per aberrant cell

Type of radiation	Dosage, Gy	Mitotic index, %	Chromosome breaks
Gamma quanta	0,5	0,25±0,05	1,7±0,2
	1,0	0,11±0,05	1,8±0,3
	2,5	0,09±0,02	2,0±0,2
	5,0	0,04±0,01	2,4±0,3
	7,5	0,01±0,01	2,8±0,2
	Control	0,5±0,07	1,3±0,08
Protons	0,25	0,5±0,03	—
	0,5	0,2±0,04	2,5±0,5
	1,0	0,14±0,04	2,6±0,15
	2,0	—	2,6±0,2
	2,5	0,06±0,02	—
	4,0	—	2,7±0,2
	5,0	0,01±0,01	2,8±0,15
	6,5	—	3,3±0,05
	7,5	—	3,5±0,2
	Control	0,7±0,05	1,3±0,05
Helium ions	0,1	0,7±0,1	—
	0,25	0,8±0,04	—
	0,5	0,4±0,07	—
	1,0	0,15±0,03	—
	2,0	0,08±0,02	—
	4,0	0,02±0,01	—
	Control	0,8±0,07	—

Our studies failed to demonstrate appreciable differences between effects of cell depletion of the basal epidermal layer after exposure to protons, helium ions and γ-quanta in different doses. According to the criterion of cellularity of the mouse epidermis 24 h after irradiation, the RBE coefficients for heavy charged particles constituted 1.

Cytogenetic analysis of epidermal cells, which was made at the maximum of the first postradiation mitosis, revealed that the share of cells with chromosome damage after exposure to heavy charged particles increased linearly with increase in dosage, i.e., there were about 10% cells with chromosome breaks per 1.0 Gy absorbed energy (see Figure). It should be noted that the number of cells with chromosome aberrations in the skin of intact animals of the same line did not exceed 5%. Incidence of aberrant mitoses as a function of dosage of protons, helium ions and γ-quanta can be expressed in the form of regression equations (Table 2). As can be seen, in all instances there were insignificant ($P>0.05$) differences between coefficients of regression, which confirms the estimated RBE coefficients of protons and helium ions as a criterion of incidence of induced aberrant mitoses, which equal 1. In addition, we found that, as compared to the effect of γ-quanta, in epidermal cells exposed to heavy charged particles

a larger number of chromosome breaks developed, particularly with use of high doses (see Table 1). The RBE coefficient for protons constituted about 1.5 according to this criterion. Not only appearance of many cells with multiple aberrations, but the high percentage of exchange (bridge) type aberrations were distinctions of the effect of the tested particles of relativistic energy on the skin: the number of cells with bridges, with bridges and fragments was 1.2-1.5 times greater than after exposure to γ-quanta, which is indicative of more profound impairment of genetic structures of cells.



Incidence of induced aberrant mitoses in mouse epidermis after exposure to γ-quanta (1), protons (2) and helium ions (3)
X-axis, dosage (Gy); y-axis, aberrant mitoses (%)

Table 2.
Regression equations for results of counting incidence of induced aberrant mitoses in epidermal cells

Type of radiation	Regression equation
Gamma quanta	$y=(9,6\pm0,6)\cdot x$
Protons	$y=(8,1\pm1,2)\cdot x$
Helium ions	$y=(11,7\pm2,2)\cdot x$

Key: y) increment of aberrant mitoses as compared to control (%)
x) dose (Gy)

Analysis of the biological effects of protons and helium ions of relativistic energy revealed that the types of high-energy particles we used have properties in common, which were manifested by decline of mitotic actitivity of dividing cells, formation of aberrant mitoses, appearance of more chromosome breaks than with exposure to γ-quanta and higher yield of aberrations of the exchange type. RBE of protons and helium ions when assessing the state of mouse skin according to cytogenetic and cytological tests changed primarily from 1.0 to 1.6. It should be noted that RBE values of 1 and those obtained for reproductive death of epidermal cells correspond to the RBE of high-energy helium ions estimated according to the clinical signs of radiation lesion to the skin [7]. According to these data, the RBE coefficient of helium ions for erythema, dry and exudative dermatitis in the mice during a 30-day observation period, epilation and atrophy of the skin at the late stages (90th-150th post-radiation days) also equals 1. Such quantitative correspondence of RBE for cellular effects on the skin and visually evaluated clinical reaction of the skin confirms the validity of the hypothesis that the skin reaction to radiation depends, to some extent, on the state of the system of cell renewal in the epidermis [5, 6]. This is also indicated by the time frame of development of radiation reactions in the skin: at the early stages (hours, day) there is manifestation of effects on the cellular level; on the 14th-20th days, development of clinical signs of lesion (dermatitis); on the 90th-105th days, appearance of atrophy and necrosis.

Thus, exposure to protons and helium ions of relativistic energy, as well as ^{60}C γ-quanta, elicits significant damage to the skin, which is manifested at

the early stages by disturbances in the genetic system of epidermal cells. These lesions to nuclear structures of cells lead to transient or irreversible (depending on dosage) disturbances in the kinetics of cellular proliferation, which ultimately determines the skin's sensitivity to radiation. RBE coefficients for protons and helium ions were found to be 1.0-1.6 according to cytogenetic and cytological criteria of condition of the skin.

BIBLIOGRAPHY

1. Gazenko, O. G. and Kal'vin, M., eds., "Osnovy kosmicheskoy biologii i meditsiny" [Fundamentals of Space Biology and Medicine], Moscow, Vol 2, Bk 2, 1975,

2. Shapiro, I. M. and Smirnov, I. B., DOKL. AN SSSR, Vol 138, No 4, 1961, pp 945-947.

3. Cowdry, E. V., "A Textbook of Histology," Philadelphia, 1938, pp 530-531.

4. Bailey, N., "Statistical Methods in Biology," Moscow, 1963.

5. Denekamp, J., Ball, M. M. and Fowler, J. F., RADIAT. RES., Vol 37, 1969, pp 361-370.

6. Emergy, E. W., Denekamp, J. and Ball, M. M., Ibid, Vol 41, 1970, pp 450-466.

7. Leith, J. T., Schilling, W. A., Lyman, J. T. et al., Ibid, Vol 62, 1975, pp 195-215.

UDC: 629.78:[612.441.018+612.129:577.175.44

EFFECT OF FLIGHT ABOARD COSMOS-1129 BIOSATELLITE ON THYROID HORMONE LEVELS IN RAT BLOOD AND THYROID TISSUE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 30 Sep 83) pp 62-65

[Article by R. A. Tigranyan, N. F. Kalita, L. Macho, P. Langer and J. Knopp (USSR and CSSR)]

[English abstract from source] Thyrotrophin, thyroxine, triiodothyronine, and reverse triiodothyronine were measured in plasma and thyroxine and triiodothyronine in the thyroid gland of the rats flown for 18.5 days onboard Cosmos-1129. Postflight the plasma content of thyrotrophin and triiodothyronine increased and that of thyroxine decreased and the gland content of thyroxine and triiodothyronine diminished. It is postulated that in the flight animals the functional activity of the thyroid gland declined.

[Text] Histological examination of the rat thyroid following long-term spaceflights revealed some morphological signs of decline of its function [3]. At the same time, no appreciable functional changes were demonstrated in rats flown aboard Cosmos-936, in spite of the fact that they did present elevation of thyroxine (T_4) level in blood plasma [2]. The observed changes were apparently either due to decrease in utilization of thyroid hormones or decrease in activity of deiodinating enzymes. It was found that on the day of termination of 13-day flights the plasma concentration of T_4 in astronauts of the Apollo spacecraft increased, but 1 day after flight it was entirely normal [8]. Analogous findings were made on astronauts of the Skylab orbital station, in whom insignificant decrease in concentration of triiodothyronine (T_3) was demonstrated in blood plasma after completion of 28-, 56- and 84-day missions, as well as elevation of thyrotropic hormone (TTH) level [6]. The authors of [6, 8] believe that their findings are proof of increased thyroid activity. After long-term (73-185 days) missions aboard Salyut orbital station, cosmonauts also presented elevation of T_4 and a tendency toward increase in TTH content, with unchanged plasma T_3 concentration. No changes were demonstrable in cosmonauts who participated in short-term missions (7 days) in parameters characterizing functional activity of the pituitary-thyroid system [10]. This report deals with investigation of TTH, T_3, T_4 and reverse T_3 (rT_3) content of blood plasma, as well as processes of hormone biosynthesis in the rat thyroid after a flight aboard Cosmos-1129. We

thus determined the rate of repair of previously demonstrated changes with shortening of the recovery period, established the effect of repeated immobilization stress in the postflight period on the response of the tested parameters of functional state of the pituitary-thyroid system.

Methods

The studies were conducted on male Wistar-SPF (Bratislava, CSSR) rats flown for 18.5 days aboard Cosmos-1129. The animals were decapitated 6-8 h after landing and on the 6th postflight day. Some of the animals examined 6 days after the flight were submitted to 5-fold immobilization stress (for 150 min per day). Animals in the synchronous and control groups were also submitted to repeated immobilization stress. We assayed plasma levels of TTH, T_4 and T_3 by radioimmune analysis and rT_3 by the method of radioimmunochemical analysis. The thyroid was excised immediately after decapitating the animals; it was rapidly frozen in liquid nitrogen and transported in dry ice to the laboratory for analysis. A homogenate was prepared of each thyroid gland in 0.25 mℓ tris-buffer (0.04 mol/ℓ, pH 8.4) with addition of tapazole (0.001 mol/ℓ). Homogenates of thyroid specimens were incubated with the enzyme, pronase (2 mg), for 16 h at 37°C, after which 20 μℓ hydrolysate was applied to Whatman No 3 chromatography paper. The hormones were sepated in a system of n-butanol-ethanol-0.5 n. ammonia (5:1:2) by the method of ascending chromatography; concurrently, we added T_3 and T_4 standards to each specimen. After chromatography, the hormones were demonstrated with a mixture of cerium ammonium sulfate and arsenous acid anhydride, after which we cut out the appropriate segments of the chromatograms and determined hormone content on them by the method of alkaline mineralization. Statistical reliability was calculated using Student's t test.

Results and Discussion

Blood plasma TTH content in animals of the flight and synchronous experiment groups was higher 6 h after the experiment than in rats of the vivarium control; TTH in flight animals was higher than in rats of the synchronous control. On the 6th postflight day, blood TTH level in flight and synchronous groups was appreciably higher than in the control. The test with repeated immobilization stress led to increase in TTH concentration only in vivarium control rats. This parameter changed insignificantly in animals of the flight and synchronous groups (see Table).

T_4 concentration in blood of flight group rats dropped by 30% 6 h after the flight, whereas in rats used in the synchronous experiment it rose by 60%, as compared to the vivarium control. The T_4 level in flight animals was 2.27 times lower [about 4/9ths] than in synchronous control rats. Blood T_4 level 6 days after the experiment was virtually the same in all groups of rats. The test with immobilization stress revealed an elevation (by 33%) of blood T_4 level in the flight group of rats and noticeable decline in rats used in the synchronous experiment and vivarium control, by 63 and 44% respectively (see Table).

T_3 concentration in blood of flight group rats was appreciably higher both 6 h and 6 days after landing than in vivarium control rats. The blood level of

this hormone was considerably higher in rats of the synchronous experiment than in the flight group and particularly control animals. Repeated immobilization stress did not elicit changes in T_3 content of blood in the flight group of animals; however, in the synchronous experiment and vivarium control groups this parameter dropped, by 54 and 66%, respectively (see Table).

Thyrotropic hormone and thyroid hormone levels in blood plasma and thyroid gland tissue of rats (M±m)

Parameter	Animal group	1	2	3
		Blood plasma		
TTH, μunits/mℓ	VC	1,25±0,33	1,82±0,40	3,56±0,61[а]
	F	8,21±1,62[а,б]	5,30±1,29[а]	5,20±1,00
	SE	3,15±0,69[а]	5,11±0,96[а]	3,42±0,30
T_4, μg%	VC	5,36±0,16	7,42±0,58	4,16±0,40[в]
	F	3,78±0,22[а,б]	6,44±0,30	8,59±0,46[а,б,в]
	SE	8,59±0,35[а]	6,49±0,39	2,39±0,11[а,в]
T_3, ng%	VC	74,71±6,54	46,83±5,10	16,00±1,00[в]
	F	105,33±8,11[а,б]	122,36±9,21[а,б]	123,25±9,0[а,б]
	SE	259,91±12,46[а]	203,64±10,82[а]	93,55±9,69[а,в]
rT_3, ng/mℓ	VC	0,70±0,07	0,60±0,07	0,50±0,08
	F	0,62±0,07	0,53±0,08	0,52±0,08
	SE	0,50±0,07	0,46±0,07	0,44±0,06
		Thyroid tissue		
T_3, μg/10 mg tissue	VC	1,37±0,14	1,48±0,04	1,05±0,04[в]
	F	1,16±0,10[б]	1,44±0,11	1,48±0,09[а]
	SE	1,46±0,10	1,42±0,10	1,54±0,01[а]
T_4, μg/10 mg tissue	VC	1,47±0,17	1,47±0,05	1,30±0,05[в]
	F	1,09±0,10[б]	1,36±0,10	1,54±0,07[а]
	SE	1,44±0,09	1,58±0,08	1,58±0,11[а]

Key:
- VC) vivarium control
- F) flight
- SE) synchronous experiment
- 1) 6-8 h after landing
- 2) 6th postflight day
- 3) 6th day after landing + immobilization stress
- а) reliability of differences as compared to VC parameter
- б) same, as compared to SE parameters
- в) same when comparing parameters obtained on 6th postflight day and in test with immobilization stress (columns 2 and 3)

Blood rT_3 level in experimental groups of animals did not undergo any reliable changes, although there was a tendency toward decline, as compared to the control, which was more marked in the synchronous experiment animals. The test with repeated immobilization did not elicit changes in blood rT_3 concentration in any of the animal groups (see Table).

T_3 and T_4 content of thyroid tissue decreased 6 h after landing in the flight group of animals, as compared to the synchronous control. Concentration of thyroid hormones in the thyroid of experimental groups of animals 6 days after the experiment did not differ from the levels in the vivarium control group. Repeated immobilization led to decline of T_3 and T_4 in the thyroid only in vivarium control rats (see Table).

Thus, our study of parameters characterizing functional activity of the hypophysis-thyroid gland system revealed primarily changes in the same direction in both experimental groups--increase in plasma TTH and T_3 content. It should also be noted that, while the changes in TTH level were more marked in flight rats, the concentration of T_3 was subject to greater changes in the synchronous experiment group. Evidently, this change in blood TTH concentration was due to the specific effect of weightlessness on hypophyseal secretion of TTH. However, against the background of elevation of TTH and biologically more active T_3 levels in blood of flight animals immediately after landing, there was reliable decline of the other thyroid hormone, T_4, whereas in rats used in the synchronous experiment it rose. In flight rats, thyroid tissue T_3 and T_4 content decreased reliably only in comparison to parameters for animals in the synchronous experiment.

The increase in plasma concentration of T_3 could be related to the fact that the animals required the biologically more active hormone after the experiment. Several authors believe that T_3 is the only active thyroid hormone, while the biological effect of T_4 in the body could only be due to its conversion to T_3 [4]. The hypothesis has also been expounded that if the rise in T_3 level parallels decline of T_4 concentration, this change in T_3 concentration could be due to changes in T_4 metabolism [5]. We observed such changes in relative levels of T_3 and T_4 in blood in flight animals. Elevation of T_3 level, which was observed against the background of high TTH content and low T_4 concentration, and the decrease in T_3 and T_4 content of thyroid tissue in flight animals warrant the belief that the functional activity of the thyroid diminished somewhat in animals flown in space. Moreover, in the presence of diminished functional activity of the thyroid, there are conditions for development of hypercholesterolemia and hyperlipidemia [7]. This is consistent with the elevation of plasma cholesterol, triglyceride and nonesterified fatty acid levels, which we demonstrated in the flight group of rats [1]. It is also known that, when there is diminished T_4 production by the thyroid, there is decrease in inactivating capacity of glutathione-insulin transhydrogenases of the liver, which leads to elevation of blood insulin level [9], which we demonstrated in this group of rats.

The test with repeated immobilization stress enabled us to demonstrate different reactions of parameters characterizing activity of the hypophysis-thyroid system. Thus, in the flight group of animals, against the background of increased blood concentration of T_4, we failed to demonstrate changes in the other parameters, TTH and T_3. In the synchronous experiment group of animals and vivarium control, the parameters in question changed in blood in the same direction, as manifested by decline of plasma T_3 and T_4 levels. Only the rats of the vivarium control presented a decrease in hormone content of thyroid tissue. At the same time, the TTH level, according to which one can indirectly assess thyrotropic function of the hypophysis, changed in different directions: it rose in vivarium control animals and dropped in synchronous experiment rats. In all probability, exposure to weightlessness (flight group) and restricted mobility (synchronous experiment) somewhat alters the reaction of the hypophysis-thyroid system to a repeated stressogenic factor. At the same time, the reaction of this system to repeated stress differed in the flight group of animals, not only from the vivarium control, but the synchronous one, which is most probably due to the specific effect of weightlessness on reactions of this system, which are demonstrable only with use of additional stress factors.

Thus, the results of our studies are indicative of presence of some decline in functional activity of the thyroid in animals flown in space.

BIBLIOGRAPHY

1. Alers, I., Tigranyan, R. A. et al., KOSMICHESKAYA BIOL., No 2, 1982, pp 58-61.

2. Knopp, J., Macho, L., Tigranyan, R. A. et al., Ibid, No 4, 1983, pp 83-84.

3. Plakhuta-Plakutina, G. I., Ibid, No 3, 1980, pp 29-33.

4. Blanc, M. H., NEW ENGL. J. MED., Vol 297, 1977, pp 1068-1069.

5. Chopra, J., Williams, D. et al., J. CLIN. ENDOCR., Vol 41, 1975, pp 911-915.

6. Leach, C. S., Johnson, P. C. et al., AVIAT. SPACE ENVIORNM. MED., Vol 48, 1977, pp 595-597.

7. Renauld, J., Sverdil, R. C. et al., HORM. METAB. RES., Vol 6, 1974, pp 134-141.

8. Sheinfeld, M., Leach, C. S. et al., AVIAT. SPACE ENVIRONM. MED., Vol 46, 1975, pp 47-49.

9. Thomas, J. H., Davly, P. et al., CLIN. ENDOCR., Vol 5, 1976, pp 411-414.

10. Tigranian, R. A., Kalita, N. F. et al., in "Symposium on Catecholamines and Other Neurotransmitters in Stress. 3d. Abstracts," Smolenice Castle, 1983, p 90.

UDC: 629.78:574.685

PROSPECTS OF USING UNICELLULAR ALGAE PROTEIN IN BIOLOGICAL LIFE-SUPPORT SYSTEMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 7 Jul 83) pp 65-69

[Article by A. A. Antonyan, I. A. Abakumova, G. I. Meleshko and T. F. Vlasova]

[English abstract from source] The concentration, amino acid composition and biological value of proteins of unicellular algae belonging to various taxonomic groups (Chlorella, Chlamydomonas, Spirulina, Euglena) were investigated. With respect to the their characteristics, these algae hold promise as components of biological life-support systems (BLSS). Indices characterizing the protein and biomass quality and biological value were calculated. Such indices as A/E (where A is an essential amino acid and E is the sum total of amino acids), $\overline{E}/T$ (where $\overline{E}$ is nitrogen of essential amino acids and T is its sum total), amino acid number, factor of digestibility in vitro were high enough and close to the respective parameters of the reference protein. Animal experiments showed high biological value of the algal biomass and the lack of its toxic or other adverse effects. The data on the quantity and quality of protein from the unicellular algae are indicative of its high biological value and applicability to BLSS. It is suggested that the differences in the protein composition associated with various algal forms and cultivation conditions can be used to produce balanced diets by varying the portion of each form of the photoautotrophic component of BLSS.

[Text] Investigations of Chlorella by itself and as part of various models of biological life-support systems (BLSS) revealed a number of properties in unicellular algae, which render them promising for use as part of different systems [4, 6, 10, 12]. At the present time, models of systems based on algae have been developed, in which over 80% of human metabolic requirements are met due to photosynthesis of algae. In such systems, the atmosphere and water are generated, there is absorption and utilization of all of the nitrogen eliminated by man, absorption and utilization by algae and concomitant microflora of all water-soluble gas impurities from the atmosphere, and an optimum physical state of the atmosphere (aeroion composition) is maintained [13].

Such a model of the system implies that there is a stock of food for man, since the Chlorella biomass is used only in insignificant quantities in the

diet [11-14]. This is related to a number of causes and, primarily, to the limited number of algal species. None of the organisms, let alone a single plant, can be the sole source of food to satisfy the diverse dietary requirements of man, although algal biomass is notable for a high caloric value and optimum composition. We believe that the most realistic means of increasing the share of biomass in the human diet is to widen the species composition of the algal element by using forms referable to different taxonomic groups differing in biomass composition [4, 5].

For several years we investigated the quantity, amino acid composition and biological value of protein of some unicellular algae--Chlorella, Chlamydomonas, Spirulina and Euglena. There are few such data in the literature, and they are not comparable due to the differences in cultivation conditions and methods of investigation.

Our objective here was to summarize the results of studying the quantitative and qualitative composition, as well as biological value of protein from different types of algae in different taxonomic groups and, on this basis, to characterize the prospects of using it in the human and animal diets of BLSS.

Methods

We studied Chlorella Sp-k (Protococcaphyccae class, Chlorococcaceae family), Chlamydomonas reinhardii strain 449 (Isoconta class, Chlamydomonadinaceae family), Spirulina platensis (gom) geitleri strain 604 (Hormogoniaceae class, Oscilliatoriaceae family; the new classification puts it with cyanobacteria) and Euglena gracilis (Klebs) strain Z. (Eugleninae class, Euglenaceae family).

The algae were cultivated under optimum conditions for each species in an intensive culture with stabilization of the basic parameters (concentration of carbon dioxide, oxygen, temperature, intensity of illumination, pH, density of suspension, rate of mixing it, concentration of basic biogenous elements in the medium). Protein was evaluated (crude and constitutional) by total and protein nitorgen, respectively, using 6.25 as the conversion coefficient [8]. Amino acid composition of algae was determined using an automatic amino acid analyzer and ion-exchange chromatography [1]. First, the specimens of biomass were submitted to hydrolysis in 6 n HCl for 24 h at a temperature of 110°C. The biological value of protein was determined on the basis of indexes that were calculated on the basis of amino acid composition of algae [2], according to the degree of their hydrolysis by proteinases [7], as well as in a series of animal experiments (Wistar rats) following the same method of feeding them algal biomass [3, 9].

Results and Discussion

The results of our investigations revealed that all of the algal species mentioned are rich in protein. Maximum crude protein was demonstrated in Spirulina cells--60% and minimum in Chlamydomonas--37% (scaled to dry biomass) (Table 1). Constitutional protein content, determined according to protein nitrogen in biomass of Chlorella, Spirulina and Euglena was virtually the same and in the range of 45-47% dry matter, the range being 30-35% for Chlamydomonas. The

difference between crude and constitutional protein content enabled us to also determine the share of protein nitrogen, which constituted 10 to 15% for Chlamydomonas, Chlorella and Euglena, and 20-23% for Spirulina. The large share of non-protein nitrogen in Spirulina is apparently attributable to the fact that the cells of these blue-green algae contain large amounts of chromoproteins, in particular, phycobilins.

Investigation of amino acid spectrum of different forms of algae enabled us to establish that Euglena biomass is characterized by maximum amino acid content (over 55% of dry matter) and Chlamydomonas, by the minimum (33%). The sum of essential amino acids ranges from 42 to 51% (Table 2). It must be noted that the algae differ from one another in amounts of the different amino acids. For example, we demonstrated a rather high level of arginine, asparagine, lysine, threonine and tyorsine in Chlorella, arginine and alanine in Chlamydomonas. Conversely, Euglena and Spirulina cells contain large amounts of aspartic and glutamic acids, serine, methionine, leucine and valine. We were impressed by the high level of histidine in Spirulina, 7.3%, which is 6-7 times more than in the other 3 species of green algae.

Table 1. Nitrogen content (total and protein) and protein (crude and constitutional) in biomass of four species of algae

Parameter	Algae			
	Chlorella	Chlamydomonas	Spirulina	Euglena
Total nitrogen, mg/g dry matter	84,8±2,1	60,0±±3,0	97,5±3,6	90,2±3,2
Protein nitrogen, mg/mg dry matter	69,3±1,8	53,0±2,0	74,5±1,9	73,4±2,2
Crude protein, % dry matter	53,0	37,6	60,0	57,0
Constitutional protein, % dry matter	45,0	33,0	47,2	45,8

Comparative analysis of amino acid spectrum of algae also revealed that Euglena and Chlorella have identical amounts of lysine, phenylalanine and aspartic acid, whereas Euglena has lower levels of alanine, proline and glycine than Chlorella and other forms of algae.

The results obtained from the study of amino acid composition of algal proteins indicate that, as compared to other plant proteins, they are rich in sulfur-containing amino acids (methionine + cystine). They constitute 0.6-0.8% in Chlorella and Chlamydomonas and 1.4-2.2% in Spirulina, when scaled to dry biomass. Such a level of sulfur-containing amino acids, as compared to their shortage in most plants, warrants the assumption that the proteins of the algal species mentioned have high biological value and are promising for use as food and feed.

Significant differences were discovered in quantity of protein and its amino acid composition, as a function of conditions of nitrogen nutrition. For example, total amino acids ranged up to 42.0% for Chlorella with a complete

supply of nitrogen for the algae, up to 17.3% with 50% nitrogen supply, whereas essential amino acids ranged from 22.0 to 8.5%, respectively. The same patterns were demonstrated for Chlamydomonas and Spirulina.

Table 2.
Amino acid composition of protein in different algal species under conditions of continuous intensive cultivation

No	Amino acid	Amino acids, % dry matter			
		Chlorella	Chlamydomonas	Spirulina	Euglena
1	Isoleucine	1,8	0,7	3,3	2,6
2	Leucine	3,2	3,1	4,6	4,7
3	Lysine	4,3	2,9	2,2	4,1
4	Valine	1,6	2,3	3,1	3,2
5	Threonine	3,4	1,9	2,0	2,2
6	Methionine	0,5	0,4	0,9	2,1
7	Phenylalanine	2,1	1,8	2,2	2,5
8	Tyrosine	4,0	1,3	1,1	3,0
9	Cystine	0,3	0,2	0,5	0,1
10	Tryptophan	1,3	0,4	1,3	0,6
11	Aspartic acid	3,7	3,0	5,0	3,7
12	Glutamic acid	4,3	4,4	7,3	12,6
13	Serine	—	1,7	2,3	2,9
14	Proline	1,9	1,9	1,6	0,4
15	Glycine	2,3	2,4	2,6	0,9
16	Alanine	3,3	3,7	4,4	1,7
17	Histidine	0,7	0,7	7,3	1,5
18	Arginine	3,5	2,6	2,8	1,9
	Total amino acids, % dry matter	42,2	35,7	54,1	50,7
	Total essent. amino acids, % dry matter	22,6	15,0	21,1	25,4
	Total sulfur-containing amino acids, % dry matter	0,8	0,6	1,4	2,2

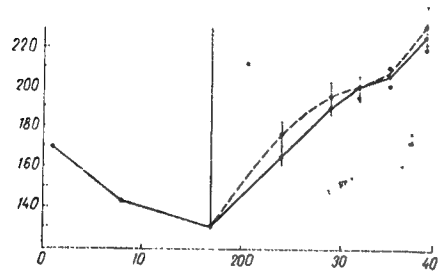
Table 3.
Some parameters (indexes) characterizing quality and biological value of protein of unicellular algae

Parameter	Chlorella	Chlamydomonas	Spirulina	Euglena	FAO/WHO 1974 standard protein
A/E:					
isoleucine	0,080	0,226	0,156	0,100	0,111
leusine	0,140	0,209	0,218	0,185	0,196
lysine	0,190	0,160	0,100	0,161	0,151
phenylalanine + tyrosine	0,271	0,209	0,156	0,216	0,169
methionine + cystine	0,035	0,040	0,066	0,086	0,098
threonine	0,150	0,160	0,094	0,086	0,111
tryptophan	0,056	0,026	0,061	0,023	0,027
valine	0,070	0,134	0,146	0,126	0,137
E/T	2,65	2,50	2,13	2,78	3,25*
Amino acid number	51	37	86	88	100
Digestibility index (according to trypsin)	42,0	34,5	70,0	58,6	100

*Casein protein.

On the basis of data on amino acid composition of algae, we calculated some indexes (Table 3) characterizing the quality and biological value of the proteins examined. One of them was the ratio of each essential amino acid (A) to total essential amino acids (E), A/E. The obtained A/E ratios were compared to the data for a standard protein specimen (FAO/WHO, 1974), which enabled us to make a comparative evaluation of the proteins studied. No appreciable differences were demonstrated between A/E of the algal proteins studied and the reference protein. Index $\overline{E}/T$, which reflects the proportion of nitrogen in essential amino acids ($\overline{E}$) in relation to their total (T) was rather high in the biomass of the algae studied, constituting 2.65 for Chlorella, 2.5 for Chlamydomonas, 2.13 for Spirulina and 2.80 for Euglena. The calculated values for $\overline{E}/T$ turned out to be quite close to those for a number of standard protein specimens, which constituted, for example, 2.25 for the FAO/WHO 1971 standard, 3.25 for casein, 2.58 for soy flour, 2.75 for millet, etc.

We also calculated the amino acid number, which is the ratio of limiting acid of the proteins studied to that of the standard protein sample. Euglena and Spirulina had an amino acid number that was close to the control. For Chlorella and Chlamydomonas it constituted 51 and 37%, respectively. According to this parameter, the quality of Euglena and Spirulina protein is close to proteins of soybeans and cotton seeds.



Dynamics of weight of animals kept on different diets
Solid line, casein group; dash line, casein 90% + Euglena 10%. X-axis, day of study; y-axis, body weight (g)

The biological value of protein of the tested algal species was also characterized according to degree of hydrolysis by proteinases. Using the method of enzymatic vulnerability of algal proteins to trypsin in vitro, we demonstrated that Spirulina and Euglena biomass had the highest digestibility, which constituted 70 and 59%, versus 40 and 37% for Chlorella and Chlamydomonas, respectively. The high digestibility of Spirulina protein is apparently due to the fact that a large part of the cellular protein of these algae is represented by the globular type of protein which, in the opinion of some researchers, have considerably higher vulnerability to proteinases, in particular, trypsin.

In addition, biological value and suitability of algal biomass was assessed in a series of experiments on animals with replacement of traditional protein in feed allowances (casein, soymeal) with algal protein. The animals were given this diet after 2 weeks without protein, when several physiological and biochemical parameters were studied, such as growth and development of animals, survival, tolerance to experimental diets, assimilation of feed, protein and carbohydrate metabolism, peripheral blood findings against the background of a control casein and soybean diet.

Inclusion of algal biomass in the diet of experimental animals, constituting 10-18% protein, did not elicit appreciable changes in the above-mentioned parameters. The dynamics of animal weight with use of casein in the diet and with partial replacement with algal protein using Euglena as an example, are illustrated in the Figure.

As a result of these experiments, we demonstrated the high biological value of algal biomass, absence of toxic and other undesirable signs in the animals and suitability of the biomass of all of the above-mentioned algal species for use as feed.

An analogous effect was obtained in studies dealing with use (partial replacement) of algal biomass, in particular, Chlorella, in human diets.

Thus, our findings concerning the quantity and composition of protein in unicellular algae are indicative of its high biological value and good possibilities of using it in human BLSS. The demonstrated differences in protein composition of different forms of algae, including differences related to

cultivation conditions, make it possible to provide balanced diets by varying the share of each species in the photoautotrophic element of the system.

BIBLIOGRAPHY

1. Andreyeva, T. F., in "Biofizicheskiye metody v fiziologii rasteniy" [Biological Methods in Plant Physiology], Moscow, 1971, p 103.

2. Vysotskiy, V. G., Yatsyshchina, G. A. and Mamoyeva, Ye. M., VOPR. PITANIYA, No 6, 1977, p 3.

3. Kremer, Yu. N., "Biokhimiya belkovogo pitaniya" [Biochemistry of Protein Food], Riga, 1965.

4. Meleshko, G. I., in "Vsesoyuznoye rabocheye soveshchaniye po voprosu krugovorota veshchestv v zamknutoy sisteme na osnove zhiznedeyatel'nosti nizshikh organizmov. 9-ye. Materialy" [Proceedings of 9th All-Union Working Conference on Circulation of Matter in a Closed System Based on Vital Functions of Organisms], Kiev, 1976.

5. Idem, in "Vsesoyuznoye rabocheye soveshchaniye po voprosy krugovorota veshchestv v zamknutoy sisteme na osnove zhiznedeyatel'nosti nizshikh organizmov. 8-ye. Materialy," Kiev, 1974, p 3.

6. Nichiporovich, A. A., Semenenko, V. S. and Vladimirova, M. G., IZV. AN SSSR. SER. BIOL., No 2, 1962, p 142.

7. Pokrovskiy, A. A. and Yertanov, I. D., Ibid, No 3, 1965, p 38.

8. Proskuryakov, N. I. and Belozerskiy, A. N., "Prakticheskoye rukovodstvo po biokhimii rasteniy" [Practical Manual of Plant Biochemistry], Moscow, 1955.

9. Rapoport, S. M., "Meditsinskaya biokhimiya" [Medical Biochemistry], Moscow, 1966.

10. Semenenko, V. B., Klichko-Gurvich, G. L. and Vladimirova, M. G., in "Rabocheye soveshchaniye po voprosu krugovorota veshchestv v zamknutoy sisteme na osnove zhiznedeyatel'nosti nizshikh organizmov. 5-ye. Materialy," Kiev, 1968, p 190.

11. Terskov, I. A., Gishekezon, I. I., Lisovskiy, G. M. et al., in "Rabocheye soveshchaniye po voprosu krugovorota veshchestv v zamknutoy sisteme. 6-ye. Materialy," Kiev, 1969, p 3.

12. Shepelev, Ye. Ya. and Meleshko, G. I., in "Vsesoyuznoye rabocheye soveshchaniye po voprosam krugovorota veshchestv v zamknutoy sisteme na osnove zhiznedeyatel'nosti nizshikh organizmov. 8-ye. Materialy," Kiev, 1974, p 146.

13. Shepelev, Ye. Ya., Meleshko, G. I., Fofanov, V. I. et al., Ibid, p 10.

14. Fofanov, V. I., Abakumova, I. A., Alekseyeva, T. A. et al., Ibid, p 42.

UDC: 629.78:574.685

INVESTIGATION OF TOXIC PROPERTIES OF PRESERVATIVES TO BE USED IN WATER RECYCLING SYSTEMS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 30 May 83) pp 70-72

[Article by G. V. Lobacheva, Z. P. Pak, N. M. Nazarov and I. V. Yakimova]

[English abstract from source] The comparative toxicity of halogen-containing oxidizing agents was investigated with the purpose of their utilization as urine preservatives in water reclamation systems. It was found that the high toxicity of the agents (LD_{50} of agent 1 was 15.7±1.1 mg/kg and LD_{50} of agent 2 was 23.0±1.2 mg/kg when injected i.p. to white mice) was distinctly related to their low pH in water solutions (pH 3-4). In neutral solutions the toxicity of agent 1 decreased 35 times and that of agent 2 12 times so that they can be classified as moderately toxic substances. Using an isolated frog heart according to Straub, it was shown that solution neutralization with 20% $NaHCO_3$ also decreased the toxic effect of the above agents, making them similar to chloramine B, a well-known disinfectant. The above agents were found to be rapidly inactivated when stored in low concentrations and to remain highly stable when stored in concentrated solutions.

[Text] The problem of searching for preservatives of liquid human waste is a difficult task, since there are many requirements [5]. According to the results of microbiological studies, agents in the oxidant group are promising preservatives, including haloid-containing organic compounds with the following general structure: R_1-Cl (No 1), R_2-Cl_2 (No 2), R_2-Cl (No 3) and R_1-I (No 4). These preservatives have high antimicrobial activity, a wide spectrum of antimicrobial action (bactericidal, fungicidal and sporocidal), they provide for long-term storage of urine and stabilization of quality of the primary regeneration product going into the treatment column unit. The agents do not corrode materials used in water regeneration systems (WRS) and they do not lose their preservative properties.

Since we still have no direct chemical method of demonstrating the tested compounds in an aqueous medium, it is quite important to perform biological testing, which permits determination of parameters of toxicity and its possible dynamics during the period of operating recycling systems.

We are submitting here the results of a comparative study of the toxicity of halogen-containing agents referable to the oxidant group as related to storage time, concentration of solutions and medium pH.

Methods

We tested acute toxicity of agents No 1 and No 2 on mongrel male mice weighing 20-25 g, with intraperitoneal injection of the agents. The experiments were set up by the method of O. N. Yelizarova [2]. The results of determining LD_{50} were processed by the method of probit analysis according to Miller and (Teynter) [1].

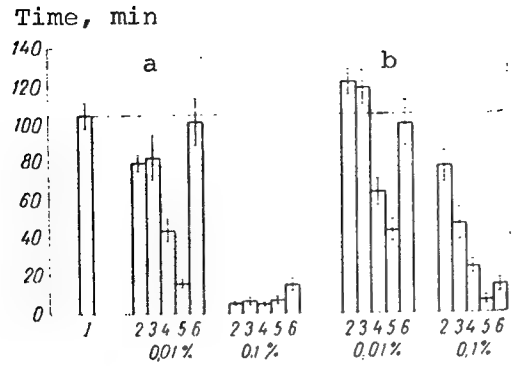
Investigation of comparative toxicity of the four new halogen-containing agents, as well as of the known disinfectant, chloramine B, was conducted on the isolated frog heart (8-10 per group) according to Straub, because of its simplicity and high sensitivity. The tested concentrations of the agents (0.001, 0.01 and 0.1%) were prepared in Ringer's solution (0.65% NaCl in distilled water), which served as the control in these experiments. Concentrations of 0.01 and 0.1% were also tested in a medium with neutral reaction (pH 7), which was obtained by addition of 20% sodium hydrocarbonate solution.

We performed 30- and 60-day experiments on mongrel white mice (10 animals per group) to investigate storage time of agent No 1 as a function of concentration, using concentrations of 0.25 and 1.5%. We tested agents No 1 and No 2, which had been stored for 30 and 90 days, in concentrations of 0.001, 0.01 and 0.1%, and concentrated solutions of agent No 1 (1.5%) and No 2 (15%) on the isolated frog heart (8-10 per group). Just prior to the experiment, 0.1% solutions were brought to pH 7 with 20% $NaHCO_3$. From the concentrated solutions we also prepared 0.1% solutions at pH 7. The results were processed by the conventional methods of variation statistics for small samples [3].

Results and Discussion

In concentrations of 0.001%, the tested agents had no adverse effect on the function of the isolated frog heart. According to the data illustrated in the Figure [5], 0.01% solutions of the agents depress heart function with statistical reliability ($P<0.05$). Compounds with similar chemical structure, No 1 and No 4, No 2 and No 3, have similar toxicity. In this concentration, chloramine B has no adverse effect on the parameter studied. In 0.1% solution, there were no longer any differences between toxicity of all the agents and chloramine B. It should be noted that a concentration of 0.1% also had marked bactericidal and preservative effects.

With increase in concentration of solutions of the tested compounds, medium acidity increases (pH is 5, 4 and 3 with 0.001, 0.01 and 0.1% solutions, respectively). The pH was close to 7 for solutions of all tested concentrations of chloramine B. In order to rule out the influence of pH on the tested parameter, the 0.01 and 0.1% solutions were neutralized with sodium hydrocarbonate. In preliminary experiments, we found no appreciable effect of $NaHCO_3$ in the quantities used on function of the isolated frog heart (the value was 50.9 ± 4.9 min in the experiment and 60.1 ± 3.8 min in the control; $P>0.05$). The results of these experiments are illustrated in the Figure.



Effect of halogen-containing compounds on contraction time of isolated frog heart (in min)
a) without neutralization of solutions (pH 3-4)
b) with neutralization (pH 7)
1) control
2) agent No 1
3) agent No 4
4) agent No 2
5) agent No 3
6) chloramine B

After eliminating the effect of medium pH, contraction time of the isolated frog heart increased, with statistical reliability ($P>0.05$) in 0.1 and 0.1% solutions of all tested agents, with the exception of No 3 in a concentration of 0.1%. The toxicity of halogen-containing compounds increased in the following order: No 1 < No 4 < No 2 < No 3. This pattern is also inherent in solutions that are not neutralized. In a concentration of 0.01%, chloramine B is similar in toxicity to agents No 1 and No 4, and in a concentration of 0.1%, to compounds No 2 and No 3.

Further tests were made of the two agents that had been studied the most and were the most promising of this group in the microbiological respect, No 1 and No 2.

We can conclude the following from the data listed in Table 1. According to the classification of toxic substances approved by the PKD [expansion unknown] section [4], the tested agents are referable to highly toxic substances. Agent No 1 was more toxic, with statistical reliability ($P<0.001$) than agent No 2. According to biological tests, agent No 2 is more resistant to changes in medium reaction in the alkaline direction than No 1 (and the activity of agent No 2 diminishes to 1/12, that of No 1, to 1/35). The differences in values is also statistically reliable ($P<0.001$). Studies of shelf life of agent No 1 in different concentrations, where the criterion of toxicity was LD_{50} for mice, revealed that in concentrated solution the agent remains active for 60 days of the experiment. When stored in a concentration of 0.25%, it gradually loses activity (by 40% on the 7th day and 100% on the 30th day). This is indicative of stability of the compound in concentrated solution and diminished toxicity in diluted solution.

Table 1. Parameters of acute toxicity of chlorine-containing compounds [sic]

Parameter of toxicity	Agent No 1		Agent No 2	
	pH 3—4	pH 7	pH 3—4	pH 7
LD_{50}, mg/kg	15,6 1,1	560 4,8	23,0 1,2	176,7 12,2
Minimum active dosage, mg/kg	10,0	500,0	17,5	220,0
LD_{100}, mg/kg	25,0	700,0	35,0	280,0
Range of active doses, mg.kg	15,0	200,0	17,5	160,0

Table 2 lists the results of experiments with storage of solutions of agents No 1 and 2, in which contraction time of the isolated frog heart served as an indicator of toxicity. According to the obtained data, both agents retain activity for 90 days, in both concentrated solutions and in a concentration of

0.1%. In low concentrations (0.001 and 0.01%), agent No 2 loses its activity by the 30th experimental data. Agent No 1 is more stable than No 2 when stored in aqueous solutions at pH 4-5. The shift of pH to 7 in 0.1% solution of agent No 1 leads to decline of activity, and comes close to the toxicity of 0.01% solution. The solution of agent No 2 retains its toxic properties with shift of pH in the alkaline direction, in accordance with increase in its concentration. This is consistent with the determinations of acute toxicity expressed as LD_{50}, according to which agent No 2 is more resistant to change in medium reaction in the alkaline direction than agent No 1.

Table 2. Effect of concentrations and storage time of solutions of chlorine-containing [sic] compounds on contraction time of isolated frog heart (min)

Agent	Storage time	Concentration (%) and pH of stored solutions			
		0.01 pH 5	0.01 pH 4	0.1 pH 7	concentrated solutions (0.1% dilution), pH 7
No 1	Without storage	100,0±5,6	78,0±4,1	77,8±7,8	79,3±5,1
	30 days	109,9±10,5	68,0±4,3	70,4±6,2	—
	90 days	120,9±11,4	—	85,4±6,7	81,7±5,8
No 2	Without storage	107,0±5,9*	42,6±5,3*	23,9±3,0*	22,9±2,0*
	30 days	107,8±5,0**	88,8±7,7**	23,3±2,4*	—
	90 days	123,3±6,2	—	21,3±2,6*	22,1±1,8*

Note: Contraction time 103.8±6.6 min in the control.
The pH did not change during storage.

*Statistically reliable difference from control ($P<0.05$).
**Statistically reliable difference from solution without storage ($P<0.05$).

On the basis of our findings, it can be concluded that the high toxicity of the tested compounds is determined largely by the low pH produced when they are diluted. In the case of a neutral medium reaction, substances in this group can be classified as moderately toxic. Agents No 1 and No 2 stand out because of their high stability during storage in the form of concentrated solutions. Agents stored in low concentrations are rapidly inactivated.

These changes in toxic properties of the compounds studied can be taken into consideration when using them in WRS, from the standpoint of improving toxicological safety in the case of penetration of microquantities of preservative of the base product into potable recycled water. The obtained data should also be borne in mind in determining the conditions for use of halogen-containing agents of the oxidant group as preservatives in systems requiring long-term storage of urine.

BIBLIOGRAPHY

1. Belen'kiy, M. L., "Elementy kolichestvennoy otsenki farmakologicheskogo effekta" [Elements of Quantitative Evaluation of Pharmacological Effects], 2d ed., Leningrad, 1963.

2. Yelizarova, O. N., "Opredeleniye porogovykh doz promyshlennykh yadov pri peroral'nom vvedenii" [Determination of Threshold Doses of Industrial Toxic Agents When Ingested by Mouth], Moscow, 1962.

3. Kaminskiy, L. S., "Statisticheskaya obrabotka laboratornykh i klinicheskikh dannykh" [Statistical Processing of Laboratory and Clinical Data], 2d ed., Leningrad, 1964.

4. Tolokontsev, N. A. and Filov, V. A., eds., "Osnovy obshchey promyshlennoy toksikologii" [Fundamentals of General Industrial Toxicology], Leningrad, 1976.

5. Chizhov, S. V. and Sinyak, Yu. Ye., "Vodoobespecheniye ekipazhey kosmicheskikh korabley. (Problemy kosmicheskoy biologii. t. 24)" [Water Supply for Spacecraft Crews (Problems of Space Biology, Vol 24)], Moscow, 1973.

UDC: 629.78:[574.685.628.38

RELEVANCE OF WATER STRUCTURE TO ASSESSMENT OF QUALITY OF RECYCLED WATER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 6 Sep 83) pp 73-76

[Article by V. A. Kondratyuk]

[English abstract from source] Among the physicochemical methods used to measure ion hydration in water solution, the most informative are those employed to evaluate the energetic state of the water molecule (swelling heat, gelatination, UV-spectrophotometry). These data may yield information about the water structure to be used in estimating the quality of potable water of different origin. IR-spectrophotometry and x-ray diffraction analysis are of lower informativity. A certain correlation has been found between the structure and biological action of water.

[Text] Fluid intake is one of the basic functions of the human body. Man's exploration of deep seas and space would be impossible without solving the problem of obtaining a good quality of water. GOST 2874-73, "Potable Water," is the criterion of water quality; according to it, "the composition and properties of water ... must assure its epidemiological safety, harmlessness of chemical composition and good organoleptic properties." However, the properties of water, like those of any other substances, are not determined only by chemical composition, but also by structure. At the same time, the structure of water is virtually not considered when setting standards of its quality. This is probably related to the absence of clear enough theory and adequate investigative methods.

Previously, the water in the body was considered as a more or less neutral medium filling the space between structural elements of the cell. In actuality, water constitutes a unified system with structural elements, in which electron excited states are possible. The physiological properties of animal and plant cells, as well as microorganisms, under normal and pathological conditions, their resistance to various factors also depend significantly on the quantity and state of biological water [4, 6, 11, 12]. At present, it is believed that the structure and state of protoplasm are determined not only by its high polymer (colloid) components, but water contained in it, which forms an integral system with the above-mentioned components [14].

The question of the condition of water in living tissues is presently one of the basic problems of biology. Approaches to solving such important problems of physiology as transport of matter in cells, transfer of energy, etc., depend on the state of water in tissues.

Proteins, nucleic acids and nucleoproteins constitute an integral system with water, which cannot be separated into components. One must take into consideration the special, unique properties of water [7, 18].

The physicochemical aspect of water structure has been studied in several works [9, 13, 16, 18]. However, there are still no conventional theoretical validations. Regardless of the scheme of water structure that is taken as the basis, even now it can be stated with certainty that water consists of at least two structural modifications, open (on the order of the shell of ice or a cluster) and densely packed areas, which depend on the distinctions of hydrogen bonds. The energy and hydrogen bonds will determine its biological activity [2, 8, 16].

With respect to hygiene, the change in water structure under the influence of ions is of special interest. The effect on water structure of a small ion that is inscribed in the openwork structure of a water molecule and of a large one that is not inscribed in it will be different. The magnitude and sign of ion charge have a strong effect on water structure. Its electrostatic field will strive to orient the dipoles of the water molecule radially near it. At the same time, as it redistributes charges in the water molecules themselves, the ion will enhance their H bonds with adjacent molecules, thereby stabilizing the ordered structure [9]. The energy of hydration of ion solutions depends on the size of the charge and nature of ions. Such biologically important ions as Li^+, Na^+, Cu^{2+}, Mg^{2+}, Ba^{2+}, Mo^{2+}, Al^{3+}, slow down the mobility of water molecules, i.e., they are positively hydrated. K^+, NH_4^+, Rb^{2+}, Cs^+, Cl^-, Br^- and I^- ions increase molecular mobility, i.e., they are negatively hydrated. The ions cause substantial structural disturbances in water molecules.

In turn, due to short-acting forces of interaction (water-water), water has a strong effect on the properties of ions. This applies in particularly to very diluted solutions, which is often the case in biological systems. Formation of bonds between water molecules reduces ion hydration and, conversely, dissociation of bonds (water-water) leads to intensification of ion hydration. As for long-acting forces, there is a hypothesis to the effect that impairment of the close order of water molecules in the area of short-acting forces is transmitted through the system of hydrogen bonds over the entire mass of water [3, 15]. There is information to the effect that a change in macromolecular hydration under the influence of stabilization or destruction of structure of the water molecule is very important to biological processes [10].

Some authors [1, 2] view structural distinctions of water in tissues as the cause of high mobility of electrons, protons or atoms of hydrogen in biological systems. The structure of water, which controls proton activity on the membrane, has some influence on its permeability. In this case, water plays the part of a line of communication through which the mechanism of distant action is effected. It may be involved in controlling the size of hydrophil pores, in transport of electrons and protons and in metabolic processes [8].

We were impressed by the fact that ions with different signs of hydration are antagonists in many metabolic processes and have different capacities for penetrating cell membranes. The different hydration of Na^+ (+ hydration) and K^+ (- hydration) plays a definite part in the biological specificity of their action. Thus, different rates of diffusion of sodium and potassium through cell membranes are attributed to difference in hydration [14]. The distribution of calcium in muscle fibers is similar to the distribution of sodium with respect to several features. In many enzymatic processes, potassium is an antagonist, not only of sodium, but calcium, magnesium, lithium and zinc.

One of the conditions for life support and preservation of human work capacity, in space also, is availability of a sufficient amount of good potable water.

Modern methods of recycling water from liquid-containing products make it possible to recover potable water of a rather high quality. Purified and treated water samples conform to the standards imposed for potable water in water-supply systems with respect to chemical composition and bacteriological parameters. At the same time, we still cannot clearly determine what regenerated water is, how it differs from natural water and what the significance this has to consumers. The nature of ion hydration and structure of the water molecule are not considered anywhere. For this reason, we tried to assess the molecular structure of 5 samples of recycled water recovered with use of ion-exchange resins (KU-2-12 nr, AV-17-HCO_3, PAU, MP-16 and SP-6c, examples Nos 1-5, respectively) [5, 17].

Results and Discussion

The water conformed in quality to GOST specifications (Table 1). Viscosity of water as related to its quality does not change appreciably, as can be seen in Table 2. Electric conductivity of the tested samples of tap water was considerably higher than distilled water. As we know, the latter depends largely on electrolyte concentration in the solution.

The structure of water and degree of ion hydration are closely interrelated. Hydration effects compensate for the energy of dissociation of the crystal lattice and often are greater than this energy. Thermodynamic parameters serve as the quantitative gague of such effects. They are particularly convenient for quantitative description of hydration.

As can be seen in Table 2, the thermal effect with swelling of starch was 33% greater for tap water than distilled water. More significant fluctuations were observed in temperature of swelling of the samples of recycled water. The maximum effect was elicited by samples Nos 3 and 4, where the temperature rose by 188.8 and 211.1%, respectively, as compared to the base value. There was a less marked thermal effect in samples No 1 and 5 and the lowest in No 2.

Gelatinization, which is related to solvation of macromolecules that form the shell of the polymer when molecules of liquid penetrate into it, is also an indicator of swelling. According to weight and volume parameters, maximum water absoprtion by gelatin was noted when testing water samples No 3 and 4. Absorption in sample No 2 was the same as in tap water.

Table 1. Physicochemical composition of recycled and tap water

Parameter	Recycled water					Tap water
	№ 1	№ 2	№ 3	№ 4	№ 5	
Odor, grade	0	0	0	0	0	0
Transparency, cm	30	30	30	30	30	30
pH	7,7	8,05	7,9	7,82	7,15	7,6
Color	c/l	c/l	c/l	c/l	c/l	c/l
Chlorides, mg/ℓ	4,2	4,2	4,2	3,5	4,2	33,5
Alkali, mg/ℓ	36,6	48,8	61,0	54,9	36,6	408,7
Sulfates, mg/ℓ	10,4	38,6	24,8	62,4	88,8	37,6
Nitrite nitrogen, mg/ℓ	0	Traces	0	0	0	0
Nitrate nitrogen, mg/ℓ	0	0	0	0	0	0,2
Ammonia nitrogen, mg/ℓ	0,1	0	0	0	0	0,8
Total hardness, mg-eq/ℓ	0,8	1,6	1,7	2,1	2,3	7,6
Calcium, mg/ℓ	10,0	22,0	18,0	18,0	24,0	112,0
Magnesium, mg/ℓ	3,6	6,0	7,3	2,4	13,4	24,0
Sodium, mg/ℓ	1,6	3,2	1,9	2,5	1,1	29,5
Potassium, mg/ℓ	1,6	0,6	0,6	0,4	0,5	3,6
Phosphorus, mg/ℓ	0,01	0,01	0,01	0,01	0,02	0,01
KhPK[expansion unknown], mg O_2/ℓ	11,7	10,2	9,8	8,9	8,6	---
Permanganate oxidizability, mg O_2/ℓ	4,7	4,5	3,9	3,4	3,4	1,6
Dry residue, mg/ℓ	67,0	149,0	144,0	80,0	150,0	657,5
Silver, mg/ℓ	2,0	1,6	2,4	2,2	0,5	0

Key: c/l) colorless

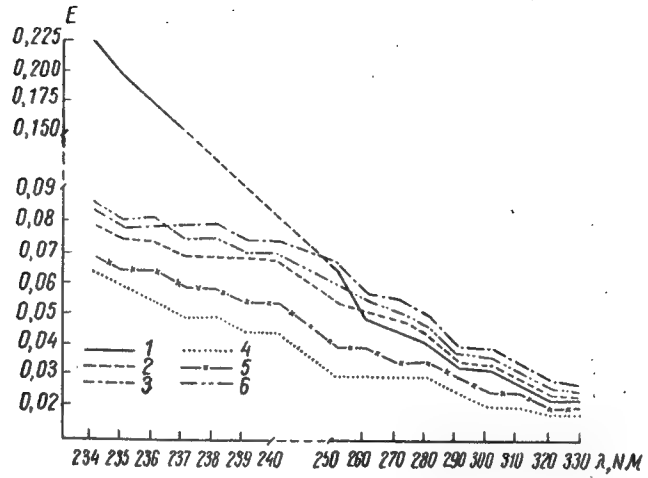
Table 2.
Characteristics of some physical parameters of different water samples

Tested water	Viscosity, mpoise	Electric conduct., Ω^{-1}	Thermal effect, C°	Degree of swelling	
				C°	cm^3
Tap water	—	—	6,0	3,6	2,5
Recycled					
№ 1	100	$4 \cdot 10^{-6}$	4,5	3,9	2,3
№ 2	101	$46 \cdot 10^{-6}$	12,0	5,1	2,8
№ 3	101	$156 \cdot 10^{-6}$	10,0	3,8	2,5
№ 4	102	$165 \cdot 10^{-6}$	13,0	6,2	3,7
№ 5	100	$93 \cdot 10^{-6}$	14,0	5,9	3,4
	101	$212 \cdot 10^{-6}$	12,0	5,7	3,2

Examination of absorption spectra in the UV [ultraviolet] region, which was made using an SF-4A spectrophotometer, indicates that the examined water samples differed considerably from tap water. The samples of recycled water had minimal extinction, particularly Nos 3 and 4, as compared to tap water (see Figure). This pattern was demonstrable to the end of the experiment. Extinction of tap water at a wavelength of 234 nm constituted 0.225, whereas that of the tested samples did not exceed 0.09. Samples Nos 3 and 4 had the lowest extinction. At a wavelength of 330 nm, extinction of all water samples, including tap water, was in the range of 0.02-0.035.

Fresh human urine, distilled and tap water, urine condensate and water recycled in new technological systems were submitted after purification to x-ray analysis on a GUR-5 unit. As shown by the results of analysis of x-rays (regardless of type of liquid analyzed), there are no differences in the roentgenological structure of molecules. This means that dissolution of salts (i.e., level of mineralization) also has no noticeable effect on

roentgenological structure of water. Evidently, there are no differences in position of hydrogen and oxygen atoms in the tested water samples. At the same time, it can be assumed that the absence of differences is attributable to the inadequate informativeness of the method used.



Absorption (extinction) coefficients of recycled and tap water

1) tape water 2-6) samples No 1-5 of recycled water

We examined the IR [infrared] absorption spectra of the above-mentioned water samples using an IR-20 instrument. The results revealed that the chemical composition of water has an insignificant effect on intensity of absorption bands. Changes in libration oscillations of water, demonstrated in the region of 600 cm^{-1}, occur as a result of impairment of the structure of water proper due to incorporation in its shell of atoms of molecules of dissolved matter.

Our findings do not enable us to definitively solve the problem set forth, but at the same time they indicate that there are differences in the molecular structure of different samples of recycled potable water.

Thus, the condition of water, according to parameters of heat of swelling, gelatinization and absorption spectra can yield some information about its energy state and be relevant to evaluation of quality of potable water of different origins.

On the basis of the foregoing, it can be assumed that the state of ion hydration in aqueous solutions must be taken into consideration when certifying recycled water. The temperature and extent of swelling of the polymer, as well as spectrophotometry in the UV range can be used as indirect methods of assessing the quality of potable water.

BIBLIOGRAPHY

1. Zatsepina, G. N., "Svoystva i struktura vody" [Properties and Structure of Water], Moscow, 1974.

2. Klotts, I., in "Gorizonty biokhimii" [Horizons of Biochemistry], Moscow, 1964, pp 339-419.

3. Koryakina, A. V. et al., TEOR. I EKSPER. KHIMIYA, No 2, 1966, pp 494-498.

4. Levi, A. and Sikevits, F., "Struktura i funktsii kletki" [Structure and Functions of Cells], Moscow, 1971.

5. Omel'yanets, N. I., "Gigiyena primeneniya ionoobmennykh smol v vodosnabzhenii" [Hygienic Aspects of Using Ion-Exchange Resins in Water Supply], Kiev, 1979.

6. Privalov, P. L., BIOFIZIKA, Vol 3, No 6, 1958, pp 738-743.

7. Idem, Ibid, Vol 13, No 1, 1968, pp 163-177.

8. Pushkar', N. S. and Belous, A. M., "Vvedeniye v kriobiologiyu" [Introduction to Cryobiology], Kiev, 1975.

9. Samoylov, O. Ya., "Struktura vodnykh rastvorov elektrolitov i gidratsiya ionov" [Structure of Aqueous Solutions of Electrolytes and Ion Hydration], Moscow, 1957.

10. Idem, in "Sostoyaniye i rol' vody v biologicheskikh ob"yektakh" [State and Role of Water in Biological Systems], Moscow, 1967, pp 5-15.

11. Szent-Gyorgyi, A., "Bioenergetics," Moscow, 1960.

12. Idem, "Introduction to Submolecular Biology," Moscow, 1964.

13. Sinyukov, V. V., "Structure of Monatomic Liquids, Water and Aqueous Solutions of Electrolyte. Historical and Chemical Analysis," Moscow, 1976.

14. Sorokina, Z. A., "State of Potassium, Sodium and Water in Cell Cytoplasm," Kiev, 1978.

15. Tikhomirov, V. I., ZH. STRUKT. KHIMII, No 3, 1962, pp 622-664.

16. Horn, G. A., "Marine Chemistry. Structure of Water and Chemistry of Hydrosphere," Moscow, 1972.

17. Chizhov, S. V. and Sinyak, Yu. Ye., "Water Supply for Spacecraft Crews," in "Problemy kosmicheskoy biologii" [Problems of Space Biology], Moscow, Vol 24, 1973.

18. Kavanau, in "Structure and Function in Biological Membranes," San Francisco, 1965, p 344.

UDC: 612.112.9:612.6].001.573:519.86

MATHEMATICAL MODEL OF CYCLIC KINETICS OF GRANULOCYTOPOIESIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 15 Jul 83) pp 77-80

[Article by O. A. Smirnova]

[English abstract from source] A model of time-course variations of granulocytopoiesis which is a system of three nonlinear differential equations has been developed. The model describes the basic stages of granulocyte development and includes the chalone mechanism regulating the proliferation of granulocyte precursors in bone marrow. Theoretical investigations applying the vibration theory and computer-aided calculations have shown that the model presents aperiodic and vibrational kinetics of reduction processes in the system of granulocytopoiesis, as well as steady-state vibrations of concentrations of mature granulocytes and their precursors (limiting cycles). The variations of the model parameters within which the above dynamic modes occur have been identified. The conditions under which the limiting cycles arise have been examined. The fact that the model simulates various experimentally observed situations suggests that it can be used to predict changes in granulocytopoiesis induced by adverse effects responsible for hemopoietic abnormalities.

[Text] Investigation of the dynamics of hemopoiesis, laws for its control and evaluation of reserve capacities of compensatory mechanisms of the hemopoietic system are very important to space biology and medicine. At the present time, much experimental material has been accumulated on these questions and there have been some important theoretical generalizations. For this reason, it has become necessary to use methods of mathematical modeling to process and analyze experimental data and to verify existing hypotheses and theories on a strictly quantitative level. Such studies have been made by G. I. Marchuk who developed models of all hemopoietic precursor elements [2], A. Ya. Monichev and M. M. Cherenkov who used methods of mathematical modeling for analysis of mechanisms of regulating bone marrow hemopoietic tissue [3], V. G. Tyazhelova whose work deals with models of postradiation recovery of hemopoiesis [6], V. V. Verigo and T. M. Smirnova who proposed a model of a population of erythrocytes circulating in blood with consideration of the age structure of these cells [3], as well as several foreign authors [8, 10].

Our objective here was to build a new model of dynamics of granulocytopoiesis and investigate the possibility of using it to describe, in addition to the usual dynamic modes, the most interesting experimentally observed phenomenon--stable fluctuations of granulocyte concentration in blood of healthy mammals [9].

Granulocytes are referable to white blood cells, leukocytes. The bone marrow stem cells are the precursors of granulocytes. Under the influence of a specific hormone stem cells are transformed into semistem, unipotent cells. The latter are capable of multiplying and, concurrently, differentiating in the direction of mature granulocytes, undergoing stages of myeloblasts, promyelocytes and myelocytes. There is a specific inhibitor of cell division, granulocytic chalone, which controls the rate of reproduction of these cells. It is believed that chalone is the product of vital functions and breakdown of this class of cells in and out of the bone marrow [4]. The next stage of granulocyte development in bone marrow is their maturation without division (metamyelocyte stage). For some time the mature cells remain in the bone marrow, creating the so-called bone-marrow reservoir, and then they migrate into blood. There is an inverse relationship between the rate of migration of granulocytes from bone marrow and the number of such cells on the periphery: the fewer cells there are, the faster the rate. The bone-marrow reservoir provides for rapid compensation of a cell shortage on the periphery. Granulocytes migrate from blood into tissues. Tissue granulocytes do not circulate, and this phase of their life is the last.

Let us form three groups of granulocyte class cells at different stages of their development. Let X be used to designate cells from the semi-stem to dividing myelocyte, Y--metamyelocytes and mature granulocytes of the "bone-marrow reservoir," Z--mature granulocytes outside the bone marrow. We shall use concentrations of X, Y and Z cells (x, y and z, respectively), as well as the concentration of specific chalone I, as variables in the model. The dynamics of changes in x, y, z and I can be described by the following differential equations, in accordance with the above-described conceptions:

$$\frac{dx}{dt} = \eta + \mu x - \gamma x - \lambda_x x, \tag{1}$$

$$\frac{dy}{dt} = \gamma x - Fy - \lambda_y y, \tag{2}$$

$$\frac{dz}{dt} = Fy - \psi z, \tag{3}$$

$$\frac{dI}{dt} = G(x + \theta_1 y + \theta_2 z) - H \cdot I, \tag{4}$$

where η is velocity of influx of cells from the stem group, γ is specific rate of change of X cells into Y, λ_x and λ_y are specific death rates of X and Y cells due to random causes, $(1/\psi)$ is mean life span of granulocyte Z outside of bone marrow, H is specific rate of chalone breakdown, G, $G\Theta_1$ and $G\Theta_2$ are specific rates of chalone production by X, Y and Z cells, respectively.

Specific rate F of migration of granulocytes into the blood stream is given with consideration of the existence of the bone-marrow reservoir in the form of a decreasing function of concentration z (L>M):

$$F = \delta(1 + Mz^2)/(1 + Lz^2), \tag{5}$$

where δ, M and L are constants. Variable $(1/\delta)$ equals the minimum or mandatory time that granulocytes spend in the maturation and reserve (Y phase) pool, while $L/(M\delta)$ is maximum time of granulocyte maturation and presence in the bone-marrow reservoir.

Specific rate μ of X cell reproduction, by analogy to the formulas of enzymatic kinetics [8], is expressed in the following form:

$$\mu = \alpha/(1 + I/K_i), \tag{6}$$

where K_i is a constant and α is maximum specific rate of X cell division.

System (1)-(4) can be simplified if we consider the difference in intrinsic times of different processes that are described by it. Thus, the results of studies dealing with isolation and use of hemopoiesis inhibitors revealed that chalones retain their activity only for a few hours [4]. Since intrinsic times of differentiation and granulocyte maturation processes in bone marrow and their life span outside bone marrow constitute several days for mammals, let us consider equation (4) "fast" in comparison to (1)-(3). Then, according to the theorem of A. N. Tikhonov [5], equation (4) can be replaced with its permanent solution, $I = G(x + \Theta_1 y + \Theta_2 z)/H$. Hence:

$$\begin{gathered}\mu = \alpha/[1 + \beta(x + \theta_1 y + \theta_2 z)], \\ \beta = G/(H \cdot K_i).\end{gathered} \tag{7}$$

The share of all stem cells constitutes $\sim 10^{-5}$ of total bone marrow karyocytes, whereas the share of X cells (myeloblasts, promyelocytes, myelocytes) equals $\sim 10^{-1}$ [7]. Parameter μ is about 1 day^{-1} [4]. Consequently $\eta \ll \mu x$ and, in the first approximation we can disregard term η in equation (1) ($\eta = 0$). Thus, the necessity of describing complex mechanisms, which are still unclear in many respects, of controlling differentiation and self-support of stem cells is eliminated. Experimental data indicate that the share of bone marrow cells that perish due to random causes is extremely small [4]. For this reason, in the first approximation $\lambda_x = \lambda_y = 0$.

In order to define the coordinates of special points, the right parts of equations (1)-(3) are equated to zero. The obtained algebraic equations are solved for x, y and z. As shown by calculations, system (1)-(3) has two special points; the first is trivial (zero) and coordinate z of the second special point is found by solving the following equation:

$$\begin{gathered}\beta\{\psi\bar{z}/\gamma + \theta_1\psi\bar{z}(1 + L\bar{z}^2)/[\delta(1 + M\bar{z}^2)] + \\ + \theta_2\bar{z}\} = \alpha/\gamma - 1\end{gathered} \tag{8}$$

The two other coordinates, x and y, are related to z as follows:

$$\bar{x} = \psi\bar{z}/\gamma, \quad \bar{y} = \psi\bar{z}(1 + L\bar{z}^2)/[\delta(1 + M\bar{z}^2)]. \tag{9}$$

According to equations (8) and (9), the coordinates of the second special point, $\bar{x}$, $\bar{y}$ and $\bar{z}$, are positive, i.e., the second special point is in the positive octant if $\alpha>\gamma$. In this case, we equate the state of system (1)-(3) in the second special point to the "normal" state of granulocytopoiesis. Thus, equations (8) and (9) specify the relationship between concentrations of X, Y, Z cells under "normal" conditions and dynamic characteristics of granulocytopoiesis.

Let us introduce dimensionless variables $x = x/\bar{x}$, $y = y/\bar{y}$, $z = z/\bar{z}$, $\tau = \gamma t$ and dimensionless parameters $a = \alpha/\gamma$, $g = \delta/\gamma$, $c = \psi/\gamma$, $l = L\cdot\bar{z}^2$, $m = M\bar{z}^2$, $b = \beta\bar{x} = (a - 1)/\{1 + \theta_1(1 + l)/[g(1+m)] + \theta_2/c\}$.

Then equations (1-3) will assume the following appearance:

$$\frac{d\tilde{x}}{d\tau} = \tilde{x}\left\{\frac{a}{1 + b[\tilde{x} + \theta_1(1 + l)\times}\right.$$

$$\left.\frac{a}{\times\tilde{y}/[g(1 + m)] + \theta_2\tilde{z}/c]} - 1\right\}, \tag{10}$$

$$\frac{d\tilde{y}}{d\tau} = g\left(\frac{1 + m}{1 + l}\tilde{x} - \frac{1 + m\bar{z}^2}{1 + l\bar{z}^2}\tilde{y}\right), \tag{11}$$

$$\frac{d\tilde{z}}{d\tau} = c\left[\frac{(1 + l)(1 + m\bar{z}^2)}{(1 + m)(1 + l\bar{z}^2)}\tilde{y} - \tilde{z}\right]. \tag{12}$$

The coordinates of special points of system (10)-(12) equal (0,0,0) and (1,1,1). The condition for presence of the second special point in the positive octant is a>1. Studies of system (10)-(12) by methods of vibration theory [1] revealed that the trivial special point is either a stable element (a<1), or a saddle (a>1). With a>1 the second special point in the positive octant is unstable (saddle focus), if the parameters of the equations are satisfied by inequalities:

$$\theta_2 > \max\{\theta_1 + (1/q)\times \times[(q + s)^2 + 2\sqrt{cq(q + s)(q + s + \theta_1)}], \tag{13}$$

$$\theta_1 + (1/q)\left[-A_2 + \sqrt{A_2^2 - 4A_1A_3}\right]/(2A_1)\Big\}, \tag{14}$$

$$A_1 > 0$$

$$1 - B_1(1 + \theta_1/q + \theta_2/c) < 1/a < 1 - B_2(1 + \theta_1/q + \theta_2/c), \tag{15}$$

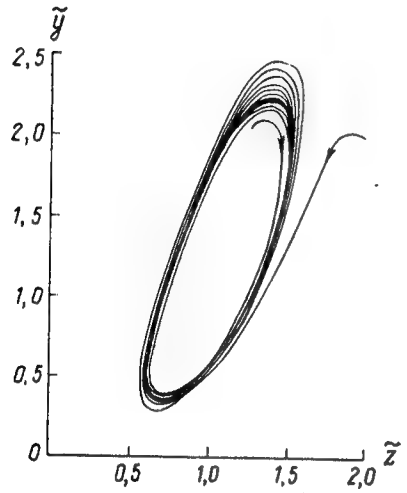
where $q = g(1 + m)/(1 + l)$, $s = c\{2(l - m)/[(1 + l)(1 + m)] + 1\}$, $A_1 = 1 - (q + s)$,

$$A_2 = -\{(q + s)^2 + [cq + \theta_1(c + q)]\times[2(q + s) - 1]\},$$

$$A_3 = -\{(q + s)^2[cq + \theta_1(c + q)] + (q + s)[cq + \theta_1(c + q)]^2 + cq(q + s + \theta_1)]\},$$

$$B_{1,2} = \{-[(q + s)^2 - q(\theta_2 - \theta_1)] \pm \pm\sqrt{[(q + s)^2 - q(\theta_2 - \theta_1)]^2 - 4cq(q + s)\times \times(q + s + \theta_1)}\}/(2(q + s + \theta_1)).$$

The physical sense of these equations consists of the following. The second special point loses stability if control of X cell reproduction is determined primarily by the inhibitor produced by Z cells [see equation (13)], maximum specific rate of reproduction of X cells is within certain limits determined by (15), while the time cells spend in the Y pool is long [see (14)]. In complying with (13)-(15), system (10)-(12) has, in addition to unstable special points (0,0,0) and (1,1,1), another special solution--a stable maximum cycle (stable fluctuations in values of variables x, y, z). The Figure illustrates projections on the phase plane $\tilde{y}\tilde{z}$ of integral curves that converge toward the maximum cycle. This is the result of computing equations (10)-(13) on a computer. The values of parameters a, g, c, m and l were determined from data in the literature concerning granulocytopoiesis in man [4]. The values of unknown coefficients Θ_1 and Θ_2 were chosen in accordance with equations (13)-(15). The period (T = 51 days) and amplitude (A_z = 0.425) of fluctuation of granulocytopoiesis coincide in order of magnitude with the corresponding characteristics of fluctuations in concentration of blood granulocytes in healthy people [9].



Phase portrait of system (10)-(12) equations

Results of calculation on a computer of the system of equations with parameters a = 4.8, g = 0.4, c = 0.2, m = 0.33, l = 1.12, Θ_1 = 0.5, Θ_2 = 10 and base data $\tilde{x}(0) = 2$, $\tilde{y}(0) = 2$, $\tilde{z}(0) = 2$, and $\tilde{x}(0) = 2.196$, $\tilde{y}(0) = 2.048$, $\tilde{z}(0) = 1.245$. X-axis, dimensionless concentration of $Z(\tilde{z})$ cells; y-axis, dimensionless concentration of $Y(\tilde{y})$ cells. Arrowheads show direction of movement of representative point over integral curves. Closed curve is projection of maximum cycle on phase plane $y\tilde{z}$.

With impairment of at least one of the conditions of (13)-(15) the maximum cycle disappears, while special point (1,1,1) becomes either a stable element or stable focus. With deviations of variables $\tilde{x}$, $\tilde{y}$ and $\tilde{z}$ from this point, the dynamic curves return to it either aperiodically or with fluctuations. Equations (13)-15) give the bifurcation "subdiversity" [typo for subset?] in the space of parameters if the signs of inequality are replaced with equal signs.

Thus, a model has been developed of the dynamics of granulocytopoiesis which consists of a system of three nonlinear differential equations. It reflects the main stages of development of cells of the granulocyte class and takes into consideration the chalone mechanism of control of reproduction of precursors of granulocytes in bone marrow. Studies by methods of fluctuation theory and mathematical calculations on a computer revealed that the model describes aperiodic and fluctuating kinetics of recovery processes in the system of granulocytopoiesis, as well as stable fluctuations of concentrations of mature granulocytes and their precursors (maximum cycles). We have found the ranges of change in model parameters, with which the above-mentioned dynamic modes are observed. The conditions for appearance of maximum [limiting]

cycles are interpreted. The model's simulation of the diversity of experimentally observed situations is indicative of the feasibility of using it for predicting the dynamics of mammalian granulocytopoiesis with exposure to deleterious factors that induce deviations from normal in the hemopoietic system.

BIBLIOGRAPHY

1. Andronov, A. A., Vitt, A. A. and Khaykin, S. E., "Teoriya kolebaniy" [Theory of Fluctuations], Moscow, 1981.

2. Marchuk, G. I., "Matematicheskiye modeli v immunologii" [Mathematical Models in Immunology], Moscow, 1980, pp 134-206.

3. "Mekhanizmy regulyatsii v sisteme krovi" [Regulatory Mechanisms in the Blood System], Krasnoyarsk, 1978, pp 20-21, 207-208.

4. Fedorov, N. A., ed., "Normal'noye krovetvoreniye i yego regulyatsiya" [Normal Hemopoiesis and Its Regulation], Moscow, 1976.

5. Tikhonov, A. N., MATEMATICHESKIY SBORNIK, Vol 31, 1952, p 575.

6. Tyazhelova, V. G., in "Teoreticheskiye predposylki i modeli protsessov radiatsionnogo porazheniya organizma" [Theoretical Premises and Models of Processes of Radiation Damage to Biological Systems], Pushchino, 1975, pp 64-74.

7. Yakovlev, V. A., "Kinetika fermentativnogo kataliza" [Kinetics of Enzymatic Catalysis], Moscow, 1965.

8. King-Smith, E. A. and Morley, A., BLOOD, Vol 36, 1970, pp 254-262.

9. Morley, A., LANCET, Vol 2, 1966, pp 1220-1222.

10. Wheldon, T. E., MATHEM. BIOSCI., Vol 24, No 3/4, 1975, pp 289-305.

METHODS

UDC: 612.21+612.22]-019:599.824

METHODS FOR MEASURING EXTERNAL RESPIRATION AND GAS EXCHANGE PARAMETERS OF MACACA RHESUS MONKEYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 8 Sep 83) pp 80-82

[Article by V. I. Korol'kov, Ye. P. Gora and A. Ye. Severin]

[Text] With the development of cosmonautics, it is becoming promising to use primates, which are biological objects that are phylogenetically the closest to man, for investigation of the effects of flight factors on physiological functions.

Changes in exchange of gases and energy metabolism serve as an important indicator of dynamics of metabolism. Heretofore, primates were used for investigation of changes in respiratory function under various conditions: under the effect of x-radiation, toxic gases, smoking, allergy, asthma, etc. [5-7, 10-12]. But as yet no convenient and labor-efficient methods have been developed for studying external respiration parameters in lower monkeys.

Our objective here was to compare different methods of measuring parameters of external respiration and gas exchange in the Macaca rhesus under normal conditions and anesthesia.

Methods

This study was conducted on 10 male Macaca rhesus monkeys 2-3 years old weighing 4.6-6.4 kg. In the first series of experiments, we examined the parameters of external respiration and gas exchange on 10 waking monkeys by the closed chamber and mask methods. In the former case, fasting monkeys were put in a sealed chamber made of plexiglas 0.051 m^3 in size. A fan was installed in the ceiling of the chamber to circulate air. The input and outlet were connected to a Corning model 165 gas analyzer, which enabled us to continuously monitor changes in gas composition in the chamber. The closed chamber method enabled us to determine the following parameters: O_2 uptake, CO_2 output, respiratory quotient (RQ) and energy expenditure. With the mask method, the fasting monkey was immobilized on a wooden support in supine position. It breathed in a Douglas bag for 15 min, through the breathing mask with valves inserted in it. The mask was attached to the animal's head with rubber straps and heald with the hand to assure a tight seal. The gas composition of exhaled air was determined with the Corning gas analyzer. Pulmonary ventilation was

measured using a GSB-400 wet-gas meter. The mask method enabled us to determine minute volume (MV), normal tidal volume (NTV), respiration rate (RR), O_2 uptake, CO_2 output, RQ and energy expenditure.

In the second series of experiments, external respiration and gas exchange were tested by intubation and mask methods on 5 monkeys that were anesthetized. Before starting the experiment, the animal was given 0.2 g thiopental sodium intravenously. Absence of corneal reflex served as a criterion of depth of anesthesia. Intubation was performed under anesthesia, and the endotracheal tube was connected to a valve box that was connected through an adapter to the Douglas bag. To avoid retraction of the tongue, the monkey was immobilized on the wooden support lying on its side. Exhaled air was collected for 15 min, and the same parameters were measured as with the mask method. After removal of the intubation tube, the monkey was tested by the mask method.

Statistical processing of the data consisted of determining means according to Student. Differences were considered reliable at $P \leqslant 0.05$.

Results and Discussion

Table 1 lists the parameters of external respiration and gas exchange obtained on waking and anesthetized animals using different methods.

Table 1. Parameters of external respiration and gas exchange obtained by different methods on waking and anesthetized Macaca rhesus (M±m)

Parameter	Background (n=10)*		Anesthesia (n=5)**	
	chamber	mask	chamber	mask
Normal tidal volume, mℓ	...	40,4±19,5	22,1±6,7	20,4±12,9
Respiration rate per min	...	34,0±1,5	26,0±7,5	30,0±6,6
Minute volume, mℓ/min	...	1363,5±198,0	573,5±151,0	612,6±390,0
O_2 uptake, mℓ/min/kg	12,7±2,3	10,1±3,9	7,3±1,4	6,0±3,4
CO_2 output, mℓ/min/kg	11,9±2,0	7,4±3,3	4,2±0,9	3,5±2,6
RQ	0,94±0,06	0,73±0,5	0,58±0,05	0,58±0,3
Energy expendit., kcal/kg/day	90,7±14,4	68,7±27,4	47,4±9,0	39,3±27,6

*Means of 20 tests.
**Means of 5 tests.

As can be seen in Table 1, when using the closed chamber method the parameter of gas exchange and energy metabolism was somewhat higher than with the mask method. Under the influence of anesthesia, MV decreased by a mean of 55.1%, normal tidal volume by 49.5%, O_2 uptake by 40.4%, CO_2 output by 52.9%, RQ by 20.5% and energy expenditure by 42.7%. A comparison of data obtained under anesthesia by the intubation and mask methods failed to demonstrate reliable differences between means.

The mask method is one of the earliest methods used to examine external respiration in monkeys. In addition to parameters of gas exchange, it permits determination of parameters of pulmonary ventilation. The stress reaction of

animals is its main flaw. Experience has shown that monkeys do not get used to a mask, even when it is used many times daily in experiments [2]. Several authors report that the inhibitory reflexes of monkeys are characterized by great instability and difficulty in development [1]. It should be noted that the "dead" volume of the mask, regardless of its construction, causes ventilation difficulties in monkeys, which have a relatively small tidal volume. The psychoemotional reaction of animals to the mask is attributable to this to a significant extent. The results of our studies revealed that when a waking monkey is immobilized on a support or primatological chair and its motor activity is restricted the parameters of external respiration and gas exchange correspond to normal values obtained by other authors on waking and slightly anesthetized Macaca rhesus monkeys (Table 2).

Table 2. Parameters of Macaca rhesus external respiration and gas exchange according to data of different authors

Parameter	Source				
	Slonim et al. (n=1)*	Lees et al. [8] (n=14; mean wt. 5.8)	Keely et al. (n=21; mean wt. 4.3 kg)	Liu et al. (n=9; mean wt. 5.1 kg)	Our studies (n=10; mean wt. 5.5 kg)
Initial respir.vol., mℓ	—	43,5±8,1	27,7±6,9	38,0±15,1	40,4±19,5
RR/min	—	42,7±7,0	26,4±7,9	33,1±5,4	34,0±1,5
Minute vol., mℓ/min	—	1791,0±360	709,0±207	1256,0±561	1363,5±198
O_2 uptake, mℓ/min	43,2	55,2±49,3	—	59,0±37,2	56,1±23,8
CO_2 output, mℓ/min	30,7	—	—	54,7	41,4±20,6
RQ	0,70	0,77±0,11	—	0,78±0,54	0,73±0,05
Energy expenditure, kcal/day	—	—	—	—	380,2±160

*Mean data of 11 tests.

The chamber method is traditional for measuring gas exchange in primates [3, 4]. Unfortunately, it does not permit examination of external respiration. The relatively higher parameters of gas exchange and energy metabolism that we obtained with the closed chamber method apparently reflect the greater motor activity of the monkeys in the metabolic chamber, when they are not immobilized.

The intubation method, which was used on anesthetized animals, is the most precise and informative for comparative studies of effects of different factors. It can be used to examine respiratory parameters that cannot be measured in waking monkeys. For this reason, the method has gained wide use in laboratory practice [9]. However, it must be noted that this method is quite labor-consuming. Another negative factor is that respiratory depression occurs under the influence of anesthesia.

When discussing the advantages of some method or other during the period of preparing for and performing a spaceflight, one must proceed primarily from its feasibility. Under laboratory conditions, it is desirable to use the most informative methods, primarily the intubation one. The experience of researchers who have worked in this field has shown that there is insignificant depression of respiration under relatively shallow anesthesia [9]. The mask method, in spite of the noted flaws, is simple and convenient for examination of a large number of monkeys, as well as under conditions when it is impossible to use stationary equipment.

By virtue of the specifics of self-contained flights, it appears promising to use modifications of the closed chamber method, which permits monitoring the dynamics of gas exchange and energy metabolism of animals.

BIBLIOGRAPHY

1. Bolotina, O. P., Pavlov, B. V. and Troshikhina, Yu. G., in "Sravnitel'naya i vozrastnaya fiziologiya" [Comparative and Age-Related Physiology], Leningrad, 1968, pp 22-35.
2. Bochkarev, P. V., ARKH. BIOL. NAUK, Vol 33, No 1-2, 1933, pp 248-255.
3. Slonim, A. D. and Makarova, A. R., TRUDY SUKHUM. BIOLOGICHESKOY STANTSII AMN SSSR, Vol 1, 1949, pp 22-29.
4. Chernyshev, V. I., VOPR. ANTROPOL., No 30, 1968, pp 140-149.
5. Binns, R. and Clark, G. C., ANN. OCCUP. HYG., Vol 15, 1972, pp 237-247.
6. Brooks, P. M., Richey, E. O. and Pickering, J. E., RADIAT. RES., Vol 6, 1957, pp 430-449.
7. Hyey, J. M., Martin, J. and Bryant, L. R., J. MED. PRIMATOL., Vol 3, 1974, pp 359-364.
8. Lees, M. H., Malinow, M. R. and Parer, J. T., in "Temes de Medicina," San Paulo, 1965, pp 61-69.
9. Liu, C. T., Ph. D. and DeLauter, R. D., AM. J. VET. RES., Vol 38, 1977, pp 1843-1848.
10. Kelly, J. F., Cugell, D. W. et al., J. LAB. CLIN. MED., Vol 83, 1974, pp 738-749.
11. Patterson, R. and Booth, B. H., N.Y. ST. J. MED., Vol 71, 1971, pp 755-759.
12. Patterson, R. and Kelly, J. F., ANN. REV. MED., Vol 25, 1974, pp 53-68.

BRIEF REPORTS

UDC: 574.68:579.851.579.24

INVESTIGATION OF GROWTH RATE OF METHANE-ASSIMILATING BACTERIA IN WEIGHTLESSNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 18 Oct 83) pp 83-84

[Article by M. G. Tairbekov, G. P. Parfenov, K. Zattler, E. Krantz, L. Wunsche, A. Schlutting and G. I. Malysheva (USSR, GDR)]

[Text] Investigation of structural and functional distinctions of methane-assimilating bacteria in weightlessness is of interest from the standpoint of making practical use of them in a biological life-support system as protein producers. The distinctive feature of these bacteria is the structural complexity of their cytoplasmic membranes, which is directly related to the cell's ability to assimilate methane and synthesize protein.

Methods

Investigation of the possible effect of spaceflight conditions (primarily weightlessness) was the main objective of the "Bacterial Growth" experiment, which was performed together with GDR specialists aboard Salyut-6 orbital station.

Concurrently with the main experiment in weightlessness, there were two control experiments on the ground: at the Baykonur spaceport (USSR) and in the laboratory of the Institute of Technical Chemistry in Leipzig (GDR). Both the main and control experiments were performed with use of the Soviet onboard "microorganism cultivator" (MC) instrument. This instrument consists of a system of 9 polyethylene chambers interconnected in series with plastic tubing equipped with special clamps that control contact between the chambers. In the modified version of this instrument, which was used in our experiment, the chambers were divided into three isolated groups. As a result, it was possible to use three different strains of methane-assimilating bacteria. The first three chambers in each group served as containers for original bacterial culture. The next two were used as containers filled with bacterial culture medium during the experiment. All of the chambers in all 3 groups were first filled with a mixture of methane and oxygen (40% CH_4:60% O_2; weight 9 mg CH_4 and 26 mg O_2). All nine chambers were filled with nutrient medium and the first chambers were inoculated with bacteria in the laboratory under sterile conditions with use of a microsyringe. In the course of the experiment, the next two chambers were connected to the first one by releasing the clamps.

We selected as objectives of investigation the following strains of methane-assimilating bacteria from the collection of the Institute of Technical Chemistry:

1. Methylosinus spec. GB-21, an obligate methane-assimilating strain, with serine route of assimilation of C_1 compounds and concentric arrangement of cytoplasmic membranes.

2. Methylobacterium organophilum MB-67, a facultative methane-assimilating strain, which also has a serine route of assimilation of C_2 compounds, but the arrangement of intracellular membranes in this strain is not typical of methane-assimilating bacteria. Heretofore, it had not been possible to cultivate this strain on methane as the only source of carbon under laboratory conditions. Normal growth is observed only when methanol and methane are combined as nutrients.

3. Methylomonas methanica AB3, an obligate methane-assimilating strain with hexulose-phosphate route of assimilation of C_1 compounds. In this strain, the cytoplasmic membranes are arranged in stacks.

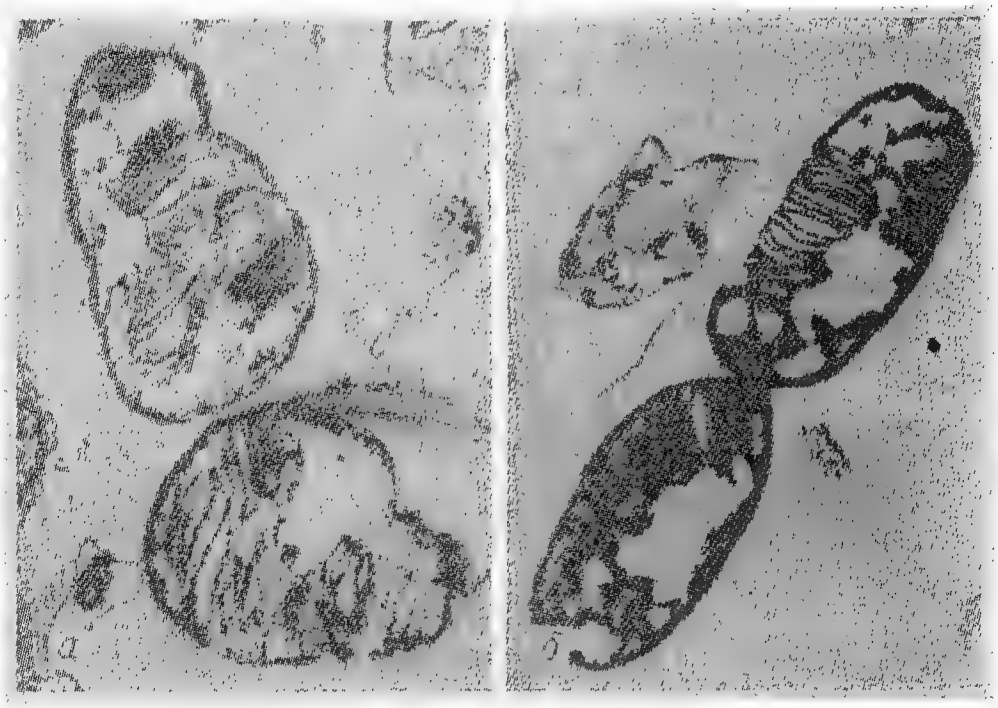
All 3 instruments (experimental and 2 control) were sterilized and filled with bacterial suspension in a concentration of 7 mg/ℓ at the Institute of Technical Chemistry, GDR Academy of Sciences. Two instruments were delivered to the launching pad at Baykonur spaceport in a container at a temperature of +4°C 2 days before the start of the experiment. On the same day, one of the instruments was stowed on the Soyuz-31 spacecraft, while the other was left on the ground for the control experiment. From that time to the start of the active part of the experiment (42 h), the cultures were kept at a temperature of 22±2°C. The experiment aboard Salyut-6 lasted 122 h and 50 min. In the course of the experiment, the GDR cosmonaut, Jaehn, performed the following operations: release of clamps No 1, 4 and 7 to provide contact between the first and second chambers in all 3 groups, release of clamps No 2, 5 and 8 for contact between the second and third chambers in all 3 groups. The control experiments on the ground (Baykonur, USSR, and Leipzig, GDR) followed the same protocol at a 5-h lag, which was required to receive information from the orbital complex about performance of the next operation.

Postflight analysis of the data was made with use of light and electron microscopy, as well as traditional methods for counting colonies in a Petri dish. Electron microscope analysis was made using the method in [2].

Results and Discussion

The results of postflight analysis of data in the laboratory revealed that growth and reproduction of the two obligate methane-assimilating strains, namely Methylomonas methanica and Methylosinus spec., proceeded normally in weightlessness and on the ground, and differed from one another. In both these strains, the bacterial cells in the third chamber corresponded to the 7th-8th generation from the start of the active experimental phase. As an example, let us indicate that the average number of cells per mℓ medium for strain Methylomonas methanica constituted $6.56 \cdot 10^8$ at the end of the experiment in weightlessness, $6.82 \cdot 10^8$

in the Baykonur control and $6.92 \cdot 10^8$ in the Leipzig control. Cell increment for this strain per mℓ medium constituted $1.82 \cdot 10^8$, $2.08 \cdot 10^8$ and $2.18 \cdot 10^8$, respectively. However, analysis of the facultative strain of Methylobacterium organophilum showed very intensive growth in the experimental variant, which is typical of obligate strains, whereas growth was not observed in the control variant with this strain.



Ultrastructure of cells of methane-assimilating strain (60,000× magnification) of Methylomonas methanica in experiment (a) and control (b)

Electron microscopy failed to demonstrate the typical arrangement of cytoplasmic membranes in the obligate strain of Methylobacterium organophilum. Analysis of electronograms of the other two strains enabled us to establish that the ultrastructural organization of bacterial cells that developed in weightlessness presented no deviations from normal whatsoever and did not differ from the other two control variants (see Figure).

Judging by the rate of cell reproduction, the conversion of the facultative strain into an obligate one in weightlessness cannot be explained at the present time. As for the physiological and genetic characteristics of bacterial cells in weightlessness, they did not differ from normal. These findings are quite consistent with the results of previous experiments, which are summarized in [1].

Thus, the results of these studies enabled us to establish that weightlessness and other spaceflight factors have no appreciable effect on growth, reproduction and ultrastructural organization of cells of methane-assimilating bacteria.

BIBLIOGRAPHY

1. Tairbekov, M. G. and Parfenov, G. P., KOSMICHESKAYA BIOL., No 2, 1981, pp 51-60.

2. Kellenberger, E., Sechard, J. and Ryfer, A., VIROLOGY, Vol 8, 1959, pp 478-498.

UDC: 629.78:612.014.481.1

PREDICTION OF CLASSES M AND X X-RAY PHENOMENA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (manuscript received 12 Jan 84) pp 84-86

[Article by O. B. Bernshteyn]

[Text] Data concerning variations in flux of solar x-radiation are needed to assure proper operation of onboard equipment of spacecraft. Such information is required to predict the state of the ionosphere, identify and predict the geoeffectiveness of interplanetary shock waves from solar flares [5], identify [8] and predict proton bursts and the radiation situation in near-earth space. Of basic interest here is to forecast x-ray solar flares, since expressly they elicit the most significant changes in flux.

The question of predicting x-ray bursts has been discussed in several works. Thus, the question of predicting class C and higher flares 24 h ahead was answered in [7], whereas the question of predicting C, M and X flares in active regions (AR) was discussed in [6]. The authors of [6] used AR characteristics as predictors. Some of the parameters could not be immediately predicted.

Our purpose was to obtain objective criteria for predicting class M and X phenomena on the basis of current incoming information. Let us recall that class M corresponds to flares with maximum flux of radiation from 10^{-2} to $9 \cdot 10^{-2}$ erg$\times$cm$^{-2} \cdot$s^{-1} in the range of 1-8 Å, and class X to flares with flux of at least 10^{-1} erg$\cdot$cm$^{-2} \cdot$s^{-1}.

The objective is to predict class M and higher flares in a given AR for the next day according to characteristics of the active region. We used only the AR characteristics that were reported daily and immediately on the routine programs of the sun service [9], namely, area of group of spots, number of spots per group, magnetic structure of group and prodrome of flare. From these characteristics we formed 10 parameters, which included both the base data and their derivatives. Thus, we formed a 10-component vector corresponding to each situation.

The problem was solved by methods of pattern recognition using a modification of the Topol' algorithm [1]. In this algorithm, it is necessary to express base information in discrete form, i.e., each coordinate of the vector can assume only a fixed number of values. We used the method of determining

extreme breakdown of parameter values into gradations. The procedure consists of the following: it is necessary to separate parameter values in such a way as to have the estimate of uncertainty (entropy) be minimal or close to minimal when making classifications with this parameter [2]. Each parameter is first separated into a large number of gradations then, by "pasting together" adjacent gradations, we obtain minimization of entropy:

$$H(\tau) = -\sum_{i=1}^{k}\sum_{j=1}^{\tau}\frac{m_j(i)+1}{l(i)+\tau}\frac{l(i)+1}{L+k}\times \log_2\left[\frac{m_j(i)+1}{l(i)+\tau}\frac{l(i)+1}{L+k}\times \times\frac{L+\tau}{\sum_{i=1}^{k} m_j(i)+1}\right], \quad (1)$$

where κ is the number of classes, τ is the number of gradations into which parameter x is divided, $l(i)$ is the number of vectors of the ith class, $m_j(i)$ is the number of vectors of the ith class, in which the value of parameter is in the jth range, $L = \Sigma l(i)$ is length of the sample. Thus, each parameter was divided into optimum gradations.

We estimated the quality of the solution rule according to the Bayes formula:

$$P(H_j/A_i) = \frac{P(A_i/H_j)\,P(H_j)}{\sum_{j} P(A_i/H_j)\,P(H_j)}, \quad (2)$$

where $P(H_j|A_i)$ is probability of occurrence of an event of the jth class provided that the algorithm refers it to the ith class, $P(A_i|H_j)$ is the share of references of events of the jth class to the ith class according to recognition test results, $P(H_j)$ is the a priori probability of the jth class. With $i = j$, we obtain the a posteriori probabilities of precise forecasts. A forecast provided for all classes can be considered satisfactory:

$$P(H_i/A_i) > P(H_i). \quad (3)$$

Let us consider that of the two solution rules, the best is the one that provides for the highest value of $Q = \Sigma P(H_i|A_i)$ when criterion (3) is satisfied. We shall consider the most informative the parameter, exclusion of which from learning and test leads to maximum worsening of recognition quality (i.e., reduction of Q). We shall call the most informative parameter of the ith class the one, exclusion of which would lead to reduction of $P(A_i|H_i)$, i.e., the share of correct references to the appropriate class. The procedure of successive exclusion of parameters is repeated for several variants of learning sequences. The estimate of comparative informativeness thus obtained has

the sense of a certain average characteristics for different variants of teaching sequences.

The sample was formed of material for 57 AR observed in 1979-1980. In all, it contained 499 vectors. The vector is the situation in a given AR on a given day. In the problem in question, we referred to the first class the vectors (days) preceding the day when there was at least one class M or higher flare in the AR. Second-class vectors constituted all other days in the AR. The sample consisted of 191 first-class vectors and 308 second-class ones. Since virtually all AR (for which the necessary information was available) were included in the sample, a priori probabilities (with 5% confidence level) constituted $P(H_1) = 0.38 \pm 0.04$, $P(H_2) = 0.62 \pm 0.04$. The learning sequence contained 70 vectors of each class and the test sequent, 90.

The a posteriori probabilities averaged for 10 variants of learning sequencies equal $\overline{P(H_1|A_1)} = 0.560 \pm 0.008$, $\overline{P(H_2|A_2)} = 0.774 \pm 0.006$, $\overline{Q} = 1.334 \pm 0.013$. These values correspond to justifiability of ~67% (68% correctly recognized 1st-class objects and 67% correctly recognized 2d-class ones). Thus, the quality of the solving rule was satisfactory for an 0.1% level of significance.

The parameter characterizing change (in comparison to the preceding day) in the ratio of area to number of spots per group, $\Delta(\frac{s}{n})$, is the most informative. The informativeness of parameter Fx--number of flares of classes M and X on the preceding (in relation to data of forecast) day--is also high. A change in quality of the solving rule with exclusion of the other parameters is statistically insignificant. Parameter $\Delta(\frac{s}{n})$ is the most informative for the 2d class, while parameter $\Delta(\frac{n}{n})$, which is the relative change in number of spots per group, is least informative for the 1st class. Exclusion of the other parameters does not lead to statistically significant change in share of correct classification of objects.

It was interesting to compare the quality of the solving rule for our (formal) forecast to results obtained with use of trivial forecasting methods. When all objects are classified in the most frequently encountered class (climatological method) we obtain zero justification for the 1st class; justification for the 2d class would have been 62% and overall, 62%.

A comparison to the inertial method shows that the formal forecast yields better (with 1% level of significance) justification for the 1st class (53% with the inertial method) and statistically insignificant worsening for the 2d class (70% with inertial forecasting). Overall justification with the inertial method is ~66%.

Unfortunately we are not able to compare the quality of our forecast with the ones put out in Boulder, United States [3, 4]. Although forecasts are made for each AR, the forecast of class M and X flares is reported for the entire sun. The results of forecasting the behavior of individual AR have not been published.

We also investigated quality of the solving rule as a function of time between the teaching and test sequences. Of course, forecasting quality

changes with change in the teaching sequence, but this difference is statistically insignificant. Thus, it can be maintained that the degree of chronological closeness of teaching and test materials, within a 2-year limit (1979-1980) has an insignificant effect.

There are quite a few works, in which it is stated that in the group of spots with Zurich class E, F there are more flares than in groups of spots of other classes. But the above-described results were obtained on a sample that included all AR, regardless of their Zurich classification. Solving rules were also obtained separately for groups of class E and F spots and groups of spots of all other classes. The quality of forecasting for the groups of class E, F spots and groups of other classes of spots was virtually the same. We did not observe any differences either in hierarchy of parameters. For this reason, when making short-term predictions of x-ray flares, it is not expedient to develop solution rules separately for groups of class E, F spots and for other classes.

Thus, we obtained objective criteria for predicting class M and X flares. Forecasting on the basis of objective criteria yields rather high justification. The fact that the indicated justification is achieved when forecasting on the basis of currently received information is indicative of the desirability of using the described method for real-time forecasting.

BIBLIOGRAPHY

1. Bernshteyn, P. B. and Burov, V. A., in "Vozniknoveniye i evolyutsiya aktivnykh oblastey na Solntse" [Appearance and Evolution of Active Regions on the Sun], Moscow, 1976, p 186.

2. Vapnik, V. N. and Chervonenkis, A. Ya., "Teoriya raspoznavaniya obrazov" [Pattern Recognition Theory], Moscow, 1974, Ch 15.

3. Simon, P. and MacIntosh, P. S., in "Observations and Prediction of Solar Activity, eds. P. M. MacIntosh and M. Drayer, Moscow, 1976, p 289.

4. Smith, J. B., Jr., Ibid, p 339.

5. Frolov, S. G., DOKL. AN SSSR, Vol 243, No 3, 1978, p 615.

6. Bartkowiak, A., Jakimiec, M. and Wasiucionek, J., PHYS. SOLARITERR, No 17, 1981, p 109.

7. Burov, V. A., Hirman, J. W. and Flowers, W. E., in "Solar-Terrestrial Prediction Proceedings," Boulder, Colorado, Vol 3, 1979, p 235.

8. Sarris, E. T. and Shawhan, S. D., SOLAR PHYS., Vol 28, 1973, p 519.

9. "Synoptic Codes for Solar and Geophysical Data," 3d revised ed., Boulder, 1973.

BOOK REVIEW

UDC: 613.693(049.32)

NEW BOOK OF SELECTED LECTURES ON AVIATION MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (signed to press 7 Dec 84) pp 86-87

[Review by V. I. Kopanev of book, "Izbrannyye lektsii po aviatsionnoy meditsine" (Selected Lectures on Aviation Medicine), by G. L. Komendantov, Moscow, Meditsina, 1983, 304 pages]

[Text] The selected lectures of one of the well-known specialists in the field of aviation medicine, Prof G. L. Komendantov, contain material on theoretical and practical bases of medical support of flights in the civil aviation. This is the first time such lectures have been published in our country. The book consists of 14 lectures dealing with the most important and difficult questions of aviation medicine which have not been fully covered in existing textbooks of this discipline. In the first two lectures, "Aviation Medicine as a Science" and "Theoretical Questions of Aviation Medicine," the author defines the subject, tasks and methods of aviation medicine, and he briefly lists the teachings that constitute the foundation of all medical science, including aviation medicine. After reading these lectures, the reader gains a clearcut idea about the fact that aviation medicine is part of general medical science and all its patterns correspond to the basic distinctions and theses of general physiology and medicine.

The next two lectures, "Physiological Bases of Work Processes" and "Problem of Fatigue," deal with the characteristics of work operations and movements. We were impressed by the sections of the lectures concerning stages of formation of work skills, as well as material on the problem of fatigue. The author dwells in detail on questions of prevention and methods of quantitative evaluation of pilot fatigue. Having described the approaches to evaluation of fatigue in flight personnel, the author noted the advantages of the method of O. P. Yakovlev, which was developed in the department that he heads. This method permits accurate and good evaluation of professional work capacity of pilots, its stability, autonomic "cost" of simulated performance. The next four lectures--"Physiology of Analyzers," "Equilibrium Function," "Physiological Bases of Spatial Orientation" and "Spatial Orientation in Flight"--are interrelated by the physiological phenomena they have in common, as well as the fact that they are discussed from the standpoint of functionally systematic analyzer function, as validated by I. M. Sechenov, I. P. Pavlov, P. K. Anokhin, I. S. Beritashvili and other researchers. The author demonstrates

convincingly that the teaching of I. P. Pavlov concerning analyzers is part of theory of central nervous system functions and that the analyzers have a direct bearing on function of the afferent part of all reflex reactions in the body. According to the lectures, equilibrium and spatial perception function is effected by the same functional system of analyzer.

Data are submitted on pathological phenomena that are observed in people under the effect of altered mechanical conditions in the lectures entitled "Effect of Changes in Atmospheric Pressure on the Body," "Barotrauma of the Middle Ear and Sinuses," "Problem of Noise in Aviation Medicine" and "Air Sickness, Part I and II." As we know, this is also the subject of aviation medicine--special pathological states. These lectures describe altitude meteorism, altitude decompression sickness, altitude tissue emphysema, barotrauma, noise trauma, air sickness and other diseases. The author dwells in detail on motion sickness. This is attributable to several circumstances, the chief one being the importance of this problem to civil aviation (motion sickness among passengers and, less often, flight personnel), and the large personal contribution to the study of this problem made by G. L. Komendantov and his disciples. The last lecture (No 14) deals with the scientific bases of special functional diagnostication, medical expert certification of flight personnel. The subject of this section is investigation of latent functional insufficiencies that have an adverse effect on flight work capacity. Special functional diagnostication provides for early prevention of functional disturbances among flight personnel, preserves a high work capacity and, consequently, helps solve effectively problems of medical support of flight safety.

As a rule, each lectures begins with an introduction and ends with a brief conclusion, in which the basic theses of the lecture are formulated in the form of theses. With such presentation there are, of course, some repetitions. But this is justified, since the book is intended primarily for individuals studying aviation medicine independently, and for them such repetition is simply mandatory for solid assimilation of the material.

Being aware of the fact that competence must always be combined with party mindedness, G. L. Komendantov briefly lists the basic theses of dialectical materialism in the lectures: principles and laws, categories, interrelated characteristics, theory of reflection and cognition (p 24), and he demonstrates in the text of the lectures high skill in using these categories for analysis of concrete materials.

A flaw of the book is that the section on "Physiological Bases of Aviation Medicine" is too brief (pp 16-21). Evidently, this is attributable to the small size of the book.

"Selected Lectures on Aviation Medicine" will, no doubt, be welcomed with interest by both specialists and individuals interested in aviation medicine; they will find broad use in educating and advanced training of physicians.

SYNOPSES OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE OF MEDICAL AND MEDICOTECHNICAL INFORMATION AND ALL-UNION INSTITUTE OF SCIENTIFIC AND TECHNICAL INFORMATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (signed to press 7 Dec 84) pp 94-96

UDC: 612.221-534.231.3:612.24-073.96

FEASIBILITY OF DYNAMIC EVALUATION OF PARAMETERS OF LUNG VENTILATION AND HEMODYNAMICS USING IMPEDANCE PNEUMOGRAPHY

[Synopsis of article by A. M. Rafikov]

[Text] Under some conditions, one should use the electrophysiological indirect method of impedance pneumography (IPG) to measure parameters of ventilation and hemodynamics of the lungs; it permits recording a single curve of fluctuations of electrical impedance of the chest. This curve consists of two types of waves: slower ones, which correspond to individual respiratory cycles, and superimposed, faster waves of pulsed filling of the lungs with blood. Respiratory fluctuations of impedance are attributable to change in gas content of the lungs at different phases of the respiratory cycle.

By analyzing the changes in these two components of IPG one can make a good estimation of the direction and extent of functional changes in external respiration and pulmonary hemodynamics, as well as relationship between them. The distinction of the proposed method is that both these parameters are measured simultaneously, by means of analysis of the two main components of one curve of impedance fluctuations plotted during spontaneous breathing.

During the breath-holding test, the respiratory component disappears and only pulse fluctuations remain, which constitute in essence the sphygmogram of central pulse, which is not recorded by means of a mechano-electric converter, but with a similar conductometric method. With our method, the IPG can be recorded on a multichannel recorder concurrently with other parameters (ECG, phonocardiogram, etc.). This makes it possible to obtain a polycardiogram and assess myocardial contractility by the method of phase analysis of the cardiac cycle.

A special series of tests involving recording the IPG and concurrent direct measurement of parameters of pulmonary ventilation by means of a turbine respirometer (volumeter) revealed that changes in the respiratory component on the IPG reflect well actual changes in volumes of pulmonary ventilation, so that this amplitude can be designated as the respiratory rheographic volume. By multiplying this parameter by respiration rate, also measured from this tracing, one can obtain the minute rheographic tidal volume.

There is the potential of processing IPG data by means of computer rather than manually for separate evaluation and expression in digital or symbolic form of both components and their dynamic relationships. The fact that all of these parameters are recorded on the IPG via one channel, in the form of a single curve that is to be submitted to analysis by means of the appropriate algorithm, is a convenience and advantage of our method. 4 Illustrations, 14 references.

UDC: 577.3

BIOLOGICAL EFFECTIVENESS OF VARIABLE MAGNETIC FIELDS IN THE RANGE OF 0.01-100 HZ

[Synopsis of article by V. B. Makeyev and N. A. Temur'yants]

[Text] A study was made of biological effectiveness of variable magnetic fields (VMF) as a function of frequency in the range of 0.01-100 Hz.

Experiments were conducted in a shielded chamber, 4×4×2.3 m in size, in which there was attenuation of external VMF to about 1/10th. VMF were generated by Helmholtz rings, which provided about 5% homogeneity of the field in the region where experimental animals were situated. The vector of fluctuations of VMF was in the horizontal plane and coincided with the animals' longitudinal axis. We tested the effect of 4.1 A/m VMF with exposure for 3 h. The control group of animals was kept in another, analogous shielded chamber during the experiment.

We tested VMF with square-wave pulses of different polarity at the following frequencies: in the range of 0.01-0.1 Hz (at 0.01 Hz intervals), in the range of 0.1-1.0 Hz (0.1 Hz), in the range of 1-14 Hz (1 Hz) and at 20, 26, 32, 44, 55, 65, 75, 81 and 100 Hz.

The tests were repeated 2-3 times at each frequency. There were at least 10 animals in each experimental group. We used a total of 1100 rats furnished by the Rappolovo Nursery in Leningrad Oblast. In the experiments, we used male mongrel rats weighing 200-220 g. Repeat experiments were performed on male Wistar rats.

The test were performed at the same time of day. The animals were decapitated immediately after exposure to VMF, and we tested blood for leukocyte count, leukocyte formula, peroxidase activity, amount of nonenzymation cation proteins (CP) in peripheral blood neutrophils, titer of complement, amount of serum lysozyme and start of blood-clotting time.

Statistical analysis was performed using the nonparametric criterion of Van der Varden, Student's criterion and multidimensional discrimenant analysis.

The results of these studies indicate that there are statistically reliable changes in the parameters studied under the effect of VMF at frequencies of 0.02, 0.06, 0.5-0.6 and 8-11 Hz. At other frequencies, VMF did not elicit statistically reliable changes in the parameters under study.

The obtained data are satisfactorily in agreement with the results of tests conducted in other laboratories.

VMF of the indicated frequencies can elicit changes in different directions in the experimental animals. Thus, under the effect of 0.02 Hz VMF, all of the parameters characterizing nonspecific constitutional resistance increased, but at a frequency of 8 Hz we observed the opposite changes, i.e., nonspecific resistance diminished.

Thus, in the range of 0.01-100 Hz, the physiologically active frequencies of VMF are 0.02, 0.06, 5-6 and 8-11 Hz. 2 Illustrations, 13 references.

UDC: 612.273+612.014.43

HUMAN TOLERANCE TO ACUTE HYPOXIA WHEN EXPOSED TO HIGH AND LOW TEMPERATURES

[Synopsis of article by A. Yu. Katkov, D. A. Sutkova, P. V. Beloshitskiy, V. A. Baraboy, T. A. Kirdeyeva and I. I. Bilyk]

[Text] A study was made of human tolerance to 20-30 min exposure to air temperatures of -15 and +100°C at altitudes of 2100 and 5600 m, simulated in a pressure and heat chamber, on a total of 30 subjects. We also tested their endurance of gradually and rapidly increasing hypoxia with rarefaction of the atmosphere and breathing nitrogen on the ground, against the background of 1-h exposure to a comfortable temperature, with air temperature fluctuations from 0 to +5°C and from +45 to +50°C. The subjects wore only slips and lightweight shoes in the thermal pressure chamber.

At different levels of hypoxia, air temperatures of -15 and +100°C elicited a moderate stress reaction in the subjects. In all cases, with the exception of heat exposure at 2100 m, there was statistically reliable elevation of blood malonic dialdehyde (MDA) immediately after the extreme exposures. After all exposures to extreme factors there was also reliable decrease in intensity of spontaneous chemiluminescence (SCL). Blood glucose level rose insignificantly. As a result of thickening of blood due to intensive dehydration in a rarefied atmosphere at 5600 m, particularly at ambient temperature of +100°C, we demonstrated a reliable increase in blood protein content.

The increase in hypoxia over the tested range did not have a noticeable effect on body temperature when cooled. In the 30 min of exposure to ambient temperature of -15°C, rectal temperature dropped by 0.6-0.8°C while skin temperature of the arm dropped by 2.2-4.1°C. Exposure to +100°C temperature was tolerated subjectively better in all cases at an altitude of 5600 m than

2100 m, which can be attributed to increased heat transfer by means of evaporation, as well as decreased heat production due to hypoxia. In 20 min of exposure to 100°C, rectal temperature rose by 1.7-2.0°C and skin temperature, by 5.0-5.3°C. At 2100 m altitude, pulsed arterial pressure rose mainly due to elevation of systolic and at 5600 m, due to decline of diastolic pressure.

At ambient temperature of 5-0°C and with rapidly increasing hypoxia, we demonstrated reliable decline of "ceiling" as compared to comfortable temperature (due to increased oxygen uptake induced by muscular tremor because of the cold). Tolerance to gradually increasing hypoxia presented virtually no change in the cold. This functional test, as in the case of comfortable temperature, was associated with decline of rectal temperature by a mean of 0.4-0.5°C. When breathing nitrogen against the background of 40-45-min exposure to cold, we observed only a tendency toward reduction of "spare time."

High air temperature in the case of increasing hypoxia was subjectively tolerated better than on the ground. In 40-45 min of exposure to high air temperature on the ground, rectal temperature reliable rose by 0.3°C, whereas with gradually increasing hypoxia it remained unchanged on the average. The "ceiling" at high ambient temperature showed virtually no difference from its level at a comfortable temperature.

Thus, it was established that moderate hypoxia, in the tested range, does not aggravate the transient effect on man of high and low temperatures. Human tolerance to extreme levels of hypoxia was notable for high stability at the tested ambient temperature fluctuations. 2 Tables, 12 references.

UDC: 612.825.4+612.014.41

EFFECT OF VOLUNTARY CONTROL OF RESPIRATION ON ELECTRICAL ACTIVITY OF THE HUMAN BRAIN DURING ADAPTATION TO ACUTE HYPOXIC HYPOXIA

[Synopsis of article by Ye. P. Gora]

[Text] A study was made of the mechanisms of influence of voluntary control of breathing on the functional state of the central nervous system (CNS), in particular, on electrical activity of the human brain (feedback), at the early stage of adaptation to hypoxic hypoxia during performance of respiratory tests for voluntary hyperventilation and voluntary breath-holding at an "altitude" of 5000 m.

We conducted breathing tests--voluntary breath-holding (Stange test) and voluntary 2-min ungraded hyperventilation--on 22 men under normal conditions and while breathing with a gas mixture containing 10.5% O_2. During the test we recorded the pneumogram (PG), electrocardiogram (ECG) and electroencephalogram (EEG).

It was found that different modes of controlled breathing (hyperventilation and breath-holding) at an altitude lead to corresponding sets of functional changes in the respiratory system, cardiovascular system and CNS; this is reflected in an integrated way by bioelectrical activity of the brain.

The EEG changes, which were associated with voluntary hyperventilation under hypoxic conditions, were less marked than under normal conditions, in spite of the fact that the ventilation level was 5-10% higher.

The EEG changes that appear during hyperventilation are usually attributed to the influence of hypocapnia on reticular structures, on the one hand, and to hypoxia of the brain due to increased tonus of cerebral vessels, on the other.

In the case of exposure to acute hypxia, the reaction of bioelectrical activity of the brain to voluntary hyperventilation is most probably due to the fact that, at the early stage of adaptation to acute hypoxia there is activation of the reticular formation of the brain stem and structures above the pons under the influence of the adrenosympathetic system. In addition, the oxygen deficiency apparently prevents, to some extent, increase in tonus of cerebral vessels, which occurs under the influence of hypocapnia.

It was established that with acute hypoxia breath-holding leads to enhancement of the hypoxic effect on the body, as can be seen from the more intensive EEG changes in a number of subjects. In addition, it is instrumental in enhancing subcortical (from the respiratory center) influences on the cerebral cortex. In some cases, this leads to manifestation of respiratory rhythms in the action currents of the cortex.

It is assumed that the dissimilar manifestation of changes in different people is indicative of differences in adaptation mechanisms. The latter must be taken into consideration when selecting a specific mode of voluntary control of breathing for the purpose of improving effectiveness of adaptation to altitude hypoxia. 1 Table, 12 references.

UDC: 629.78:612.766.1.014.482

USE OF PHYSICAL WORK CAPACITY TEST IN RADIOBIOLOGICAL EXPERIMENTS

[Synopsis of article by N. I. Arlashchenko]

[Text] Work capacity is an integral indicator of the body's functional state. Investigation of functional activity of the adrenal cortex during physical loads revealed that moderate muscular loads lead to activation of the hypothalamus-hypophysis-adrenal cortex system, while excessive ones cause its depletion. In turn, physical work capacity depends on the state of the adrenal cortex. On the other hand, it was shown that after acute exposure to radiation in lethal doses there is depletion of the adrenal cortex at the height of radiation sickness. Adrenalectomy leads to diminished animal resistance to radiation. Excessive exercise (daily swimming after exposure of animals to radiation) accelerates 2-4-fold and increases the death rate among experimental animals, as compared to the irradiated control. Thus, functional impairment of the endocrine system should apparently be considered one of the chief causes of change in physical endurance in the presence of radiation sickness. Most probably, the decrease in physical endurance,

which is the most distinct at the height of radiation sickness, is caused by the fact that physical exercise, which requires a certain level of activity of the adrenohypophyseal system, cannot be performed after exposure to ionizing radiation due to depletion of the required reserves of this system. The body's response to radiation and exhausting physical exercise is based on the same physiological mechanism of the general adaptation reaction to extreme (stressor) stimuli. Physical endurance can serve as a reliable criterion for evaluating the functional state of an irradiated organism. Its characteristics can also be used to test in radiobiological experiments the effects of various agents that enhance radioresistance. In addition. physical loads can be used as tests for studying questions of forecasting resistance to ionizing radiation. 53 References.

UDC: 612.13.014.477-063

REGIONAL CIRCULATORY CHANGES IN THE PRESENCE OF ACUTE HYPOXIC HYPOXIA

[Synopsis of article by O. A. Kovalev, V. L. Larin, V. I. Severovostokova, S. K. Sheremetevskaya, K. F. Korovin and O. N. Nepochatov]

[Text] Experiments were conducted on nonanesthetized, noninbred male white rats weighing 180-210 g, with catheters implanted in the external jugular vein. Hypoxic hypoxia was produced by placing the animals in a sealed chamber for 30 min, which was ventilated with a gas mixture of 10.5% O_2 + 89.5% N_2, or 3.5% O_2 + 96.5% N_2. To assess regional changes in resistive and capillary parts of the vascular system, we used a method, according to which the animals were given intravenous injections of ^{86}Rb then, 60 s after cardiac arrest, we isolated their organs and tissues with dissecting instruments and recorded their radioactivity. We studied changes in catecholamine content--epinephrine (E) and norepinephrine (NE) in blood plasma and tissues of several organs by the spectrofluorimetric method. Moderate hypoxia was associated with substantial decrease in uptake of ^{86}Rb in thoracic organs (myocardium, lungs), some organs of the abdominal cavity (stomach, pancreas, large intestine, kidneys, adrenals), as well as skin of the hind legs. Uptake of ^{86}Rb increased in the brain, liver, small intestine, as well as extensive areas of muscular and bone tissues of the neck, chest, posterior extremities and, to a lesser extent, abdomen and pelvis, skin of the neck, chest and forelegs.

With a severe degree of hypoxia, uptake of ^{86}Rb decreased in several abdominal organs (small and large intestine, stomach, pancreas, kidneys, spleen), as well as skin of virtually all parts of the body (only in the skin of the neck did the decrease fail to reach a level of statistical significance). The increase in ^{86}Rb uptake in the presence of severe hypoxia was observed in the brain, myocardium, muscles and bones of the chest, abdomen and pelvis.

E and NE concentration in the presence of moderate hypoxia decreased in blood and increased in the adrenals; at the same time we demonstrated an increase in NE content of the hypothalamus, myocardium, liver and gastrocnemius. With severe hypoxia, plasma E concentration did not differ reliably from the control, whereas NE exceeded it. Catecholamine level of the adrenals and hypothalamus also failed to differ from the control. 2 Tables, 10 references.

INDEX OF ARTICLES: KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA VOLUME 18, NUMBERS 1-6, 1984

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (signed to press 7 Dec 84) pp 88-91

[Text] Yuriy Alekseyevich Gagarin (Fiftieth Birthday), 2(6).

Surveys

Belakovskiy, M. S., Bogdanov, N. G., Gippenreyter, Ye. B. and Ushakov, A. S. Use of Vitamins During Adaptation to High Altitudes, 3(4).

Karpov, V. N., Galkin, A. A. and Davydov, B. I. Some Aspects of Dosimetry in Studies of Biological Effects of Nonionizing Electromagnetic Radiation, 2(7).

Kas'yan, I. I. and Makarov, G. F. External Respiration, Gas Exchange and Energy Expenditure of Man in Weightlessness, 6(4).

Krylov, Yu. V. Development of Guidelines for Setting Physiological and Hygienic Standards for Noise Levels in Aerospace Medicine, 5(4).

Khayutin, V. M., Shenderov, S. M., Zakharov, A. G. and Rogoza, A. N. Circulatory Orthostatic Instability: Role of Deconditioning of Resistive Vessels, 4(4).

Shvets, V. N., Vacek, A., Kozinets, G. I., Britvan, I. I., Korol'kov, V. I. and Chel'naya, N. A. Hemopoiesis in Rats Submitted to Weightlessness, 4(12).

Experimental and General Theoretical Research

Agadzhanyan, N. A., Yelfimov, A. I., Severin, A. Ye. and Pas, I. A. Exchange of Gases and Physical Work Capacity in Natives of Different Geographic Regions, 3(65).

Alekseyev, D. A., Zubarev, A. F., Krupina, T. N., Yarullin, Kh. Kh., Kuznets, Ye. I. and Kuz'min, M. P. Hemodynamics and Neurodynamics of the Human Brain During Exposure to Moderate Hypoxic Hypoxia, 4(81).

Bednenko, V. S., Grechikhin, G. N. and Kozlov, A. N. Evaluation of Some Hemodynamic Parameters of Pilots During Flights, 2(50).

Belakovskiy, M. S., Voskoboynikov, V. A., Gulyayev, V. N., Zakharenko, T. S., Senkevich, Yu. A., Ivanov, V. A. and Bogdanov, N. G. Diet of First Soviet Expedition on Mount Everest, 5(10).

Belakovskiy, M. S., Radchenko, N. D. and Bogdanov, N. G. Vitamin Metabolism in Cosmonauts Following Short-Term Flights, 4(19).

Belkaniya, G. S. Investigation of Adaptive Distinctions of Mechanisms of Controlling Glycemia in Macaca Rhesus Monkeys, 6(62).

Belkaniya, G. S. and Dartsmeliya, V. A. Walking Erect as a Factor in Development of Arterial Hypertension in Primates, 3(14).

Benova, D. K., Bayrakova, A. K., Bayev, I. A. and Nikolov, Kh. G. Effect of Spaceflight Factors on Rat Bone Marrow Cells, 4(41).

Bogomolov, V. V., Tabak, V. Ya., Lenskiy, V. V., Bogushevich, M. S., Stazhadze, L. L., Ivanov, G. G., Gal'chin, V. V., Kudryashova, Zh. M. and Vostrikov, V. A. Long-Term Exposure of Animals to Antiorthostasis (-90°) as a Model of Critical Homeostatic Disturbances, 5(34).

Vartbaronov, R. A., Glod, G. D., Uglova, N. N., Khomenko, M. N. and Rolik, I. S. Frequency and Nature of Electrocardiographic Disturbances in Dogs During Single and Repeated Exposure to +Gz Accelerations, 4(37).

Vasil'yeva, T. D., Vysotskaya, V. R. and Gevlich, G. I. Regional Circulation During Testing on Isokinetic Dynamometer Following 14-Day Bedrest, 5(26).

Vlasova, T. F., Miroshnikova, N. B., Belozerova, I. N. and Ushakov, A. S. Cosmonauts' Blood Plasma Free Amino Acid Levels During Preflight Training, 6(26).

Vorob'yev, V. Ye., Abdrakhmanov, V. R., Golikov, A. P., Stazhadze, L. L., Goncharov, I. B., Kovachevich, I. V., Voronina, S. G. and Babishchevich, A. V. Effect of 120-Day Antiorthostatic Bedrest on Gas Exchange and Pulmonary Circulation in Man, 5(23).

Vorob'yev, Ye. I., Gazenko, O. G., Genin, A. M., Gurovskiy, N. N., Yegorov, A. D. and Nefedov, Yu. G. Main Results of Medical Studies on Salyut-6--Soyuz Program, 2(22).

Vorob'yev, Ye. I., Gazenko, O. G., Genin, A. M. and Yegorov, A. D., Medical Results of Salyut-6 Program Long-Term Manned Spaceflights, 1(14).

Vorona, A. A., Aleshin, S. V. and Safronov, A. M. Psychophysiological Nature of "Aircraft Feel," 5(14).

Vorotnikova, Ye. V. Distinctions of Rat Lymphatic Organ Reactions to Acute Stress Factor During Hypokinesia, 5(50).

Vorotnikova, Ye. V. Distinctive Morphological Manifestations of Acute Stress Reaction in Adrenal Cortex of Hypokinetic Rats, 6(54).

Voskresenskiy, A. D., Vikhrov, N. I., Varnashenko, A. P., Doroshev, V. G., Kirillova, Z. A., Matrosova, M. A. and Chekanova, S. L. Main Component Method Used to Study Variations of Cardiovascular Parameters, 6(33).

Gazenko, O. G. Man in Space, 1(3).

Genin, A. M., Zingerman, L. S., Maksimov, D. G., Belozerov, G. Ye., Katuntsev, V. P., Obukhova, M. V., Yurova, K. S., Kheymets, G. I., Galichiy, V. A. and Finogenova, R. I. Reliability and Efficiency of Kubicek Rheographic Method for Monitoring Cardiac Output and Stroke Volume, 3(9).

Davydov, B. I., Ushakov, I. B., Tikhonchuk, V. S. and Galkin, A. A. Rat Behavior in Selection of Negative Stimulus: Pain or Exposure to Electromagnetic Field, 3(68).

Dietlein, L. F., Rambaut, P. C. and Nicogossian, A. Basic Thrusts of Biomedical Experimentation in Space Programs, 1(8).

Draguzya, M. D., Kopanev, V. I. and Lustin, S. I. Functional State and Work Capacity of Man When Breathing Oxygen and Hypoxic Mixtures Under Positive Pressure, 3(57).

Drobyshev, V. I., Antipov, V. V. and Makarov, V. V. Dynamics of Morphological Changes in Articulation Nervous System Under Hypokinetic Conditions as a Model of a Spaceflight Factor, 4(43).

Zaloguyev, S. N., Savina, V. P., Mukhamediyeva, L. N., Nefedov, Yu. G., Viktorov, A. N., Vytchikova, M. A. and Batenchuk-Tusko, T. V. Sanitary and Hygienic Features of Cabin Environment in Salyut-7 Orbital Station, 2(40).

Ivanov, L. A. and Chebotarev, N. D. Effect of Maximum Physical Load on Oxygen-Transport Properties of Blood, 4(69).

Il'in, Ye. A. Investigations on Biosatellites of the Cosmos Series, 1(57).

Il'ina-Kakuyeva, Ye. I. Morphological Study of Primate Muscle Fibers and Microcirculation During Head-Down Hypokinesia, 2(71).

Kabitskaya, O. Ye., Savik, Z. F., Kaplanskiy, A. S., Shvets, V. N., Sergeyev, I. N., Belakovskiy, M. S. and Spirichev, V. B. Effect of 1,25-Dihydroxycholecalciferol and 24,25-Dihydroxycholecalciferol on Growth and Alteration of Rat Bones During Hypokinesia (Histomorphometric Study), 4(49).

Kalandarov, S., Bychkov, V. P., Frenkel', I. D. and Kuznetsova, T. I. Effect of High Ammonia Content in Pressure Chamber Atmosphere on Human Adrenocortical System Function, 3(75).

Kalinichenko, V. V. and Zhernavkov, A. F. Cosmonauts' Postural Reactions After Long-Term Missions Aboard Salyut-6 Orbital Station, 5(7).

Kamenskiy, Yu. N. Choice of Psychophysiological Criterion to Assess Whole-Body Low-Frequency Vibration, 2(47).

Kamenskiy, Yu. N. Role of Mental Work in Human Tolerance to Total-Body Vibration, 6(37).

Kan, Ye. L., Malinovskaya, O. O., Kupriyanov, V. A. and Denisov, A. F. Investigation of Biochemical and Psychological Parameters of Air Traffic Controllers in "Prestart" State Before Beginning to Work, 5(62).

Kaplanskiy, A. S., Durnova, G. N., Savik, Z. F., Belkaniya, G. S., Popov, V. I. and Tavadyan, D. S. Morphological Study of Myocardium of Monkeys Submitted to Antiorthostatic Hypokinesia, 6(44).

Katkov, V. Ye., Chestukhin, V. V., Nikolayenko, E. M., Rumyantsev, V. V. and Gvozdev, S. V. Central Circulation of a Normal Man During 7-Day Head-Down Tilt and Decompression of Various Parts of the Body, 1(80).

Katyukhin, L. N. and Maslova, M. N. Dynamics of Red Blood Cell Changes in Rats Submitted to Acute Immobilization, 3(43).

Klimovskaya, L. D. and D'yakonov, A. S. Effect of Triphthasine and Elenium on Changes in Evoked Bioelectrical Activity of the Brain Exposed to Stationary Magnetic Field, 5(71).

Kovalev, Ye. Ye. Current Status of Radiation Protection During Spaceflight, 1(36).

Kozlovskaya, I. B., Grigor'yeva, L. S. and Gevlich, G. I. Comparative Analysis of Effects of Weightlessness and Its Models on Velocity and Strength Properties and Tone of Human Skeletal Muscles, 6(22).

Kokova, N. I. Effect of Fluid and Salt Supplements to Food Allowance on Endurance of Head-to-Pelvis Accelerations Following 7-Day "Dry" Immersion and Under Ordinary Motor Activity Conditions, 4(33).

Kolpakova, N. F. and Urmancheyeva, T. G. Circadian Pattern of Simian Functional Parameters During Hypokinesia and in the Recovery Period, 3(38).

Krotov, V. P., Bazunova, Ye. G. and Kulayev, B. S. Fluid Metabolism of Monkeys During 2-Week Antiorthostatic Hypokinesia, 6(48).

Krupina, T. N., Yarullin, Kh. Kh., Artamonova, N. P., Gornago, V. A., Alekseyev, D. A., Tsyganova, N. I., Kuz'min, M. P., Filatova, L. M., Fotina, L. A., Smirnov, O. A. and Vikharev, N. D. Functional Capacites of Elderly Subjects Exposed to Simulated Spaceflight Factors, 4(29).

Kuleshov, V. I. and Namlinskiy, Yu. V. Effect of Hyperoxia and Increased Gas Atmosphere Density on Contractile Function of the Right Ventricle, 4(73).

Kustov, V. V., Litau, V. G., Kukushkin, Yu. A. and Razinkin, S. M. Multiple Regression Method Used to Assess Animal Adaptation to Hypoxic Hypoxia, 6(67).

Lentsner, A. A., Brilis, V. I., Brilene, T. A., Lentsner, Kh. P., Shilov, V. M., Liz'ko, N. N., Syrykh, G. D. and Legen'kov, V. I. Study of Erythrocyte Adhesion in Cosmonauts, 2(38).

Leach, C. S. Biomedical Results of Studies During First Four Missions Aboard the Space Shuttle: Analysis of Body Fluids, 1(67).

Lobova, T. M., Potapov, P. P. and Chernyy, A. V. Dynamics of Some Parameters of Carbohydrate and Lipid Metabolism in Recovery Period Following Long-Term Hypokinesia, 4(55).

Luk'yanyuk, V. Yu. ±Gz Acceleration Tolerance of Individuals 41 to 58 Years of Age, 5(18).

Lhagwa, L. Circadian Rhythm of Human Heart Rate During Antiorthostatic Tests, 2(60).

Lhagwa, L. Circadian Rhythm of Human Body Temperature During Spaceflights, 6(15).

Malkin, V. B. and Landukhova, N. F. Efficacy of Conditioning Animals to Hypoxia During Sleep, 2(67).

Malkin, V. B. and Loginova, Ye. V. Oxygen Uptake as an Indicator of Animal Adaptation to Altitude Hypoxia, 5(47).

Mogutov, S. S., Sergeyeva, Ye. S. and Yevgraf'yev, V. P. Adrenal-Hypothalamus-Pituitary System Reactions in Rats Cooled in a Hypoxic-Hypercapnic Gas Atmosphere, 3(61).

Modin, A. Yu., Abrosimov, S. V., Anashkin, O. D., Zhidkov, V. V., Lobachik, V. I., Parshin, L. B. and Shashkov, V. S. Effect of Dihydroergotamine on Human Circulation During Orthostatic Tests, 3(19).

Modin, A. Yu., Sokolov, V. I., Degterenkova, N. V., Shashkov, V. S. and Gornago, V. A. Nature of Postural Changes in Human Hemodynamics With Intake of Sydnocarb Alone and in Combination With Obsidan, 5(54).

Mikhaylov, V. M., Pometov, D. Yu. and Andretsov, V. A. LBNP Training of Crew Members on Main Missions Aboard Salyut-6 Orbital Station, 6(29).

Nicogossian, A., Pool, S. L., Leach, C. S., Moseley, E. and Rambaut, P. C. Guidelines for Future NASA Medical Research, 1(29).

Nikolayev, V. P., Katuntsev, V. P., Kazakova, R. T., Yurova, K. S., Doronina, T. D., Mansfel'd, A. D., Chichagov, P. K. and Reyman, A. M. Ultrasonography of Canine Soft Tissues During Decompression, 3(52).

Nikolayenko, E. M., Katkov, V. Ye., Gvozdev, S. V., Chestukhin, V. V., Volkova, M. I., Berkovskaya, M. I. and Kediya, T. G. Human Lung Fluid Content During 7-Day Head-Down Tilt, 6(40).

Nosova, I. M., Drobyshevskaya, T. A. and Osadchiyeva, N. A. Dynamics of Changes in Metabolic and Endocrine Processes in Helicopter Crews During Commercial Flights, 2(43).

Panasyuk, Ye. N. and Skakun, L. N. Biligenic Function of White Rat Liver 4(58).

Parfenov, G. P. and Zhvalikovskaya, V. P. Chromosome Aberrations in Crepis Capillaris Exposed to Gamma Radiation and Clinostat, 5(68).

Plakhuta-Plakutina, G. I., Savina, Ye. A., Dmitriyeva, N. P., Amirkhanyan, Ye. A., Belkaniya, T. S. and Tavadyan, D. S. Structural Distinctions of Thyroid C Cells and Parathyroid Glands of Primates During Head-Down Hypokinesia, 2(73).

Pozharskiy, G. O. Effect of Living Conditions in Confined Space on Formation of Bacterial Aerosol, 3(77).

Popov, I. G. and Latskevich, A. A. Blood Plasma Free Amino Acid Levels in Cosmonauts Before and After 175-Day Mission Aboard Salyut-6, 2(26).

Popov, I. G. and Latskevich, A. A. Blood Plasma Free Amino Acids Under Hypokinetic Conditions, 3(25).

Popov, I. G. and Latskevich, A. A. Blood Amino Acids of Cosmonauts Before and After 211-Day Spaceflight, 6(10).

Popov, I. G., Lozinskiy, P. A. and Romanova, I. A. Nutritional Status as Related to Different Ways of Using Emergency Carbohydrate Rations, 3(80).

Pool, S. L. and Nicogossian, A. Biomedical Results of the Space Shuttle Orbital Flight Test Program, 1(45).

Pchelenko, L. D. and Bebyakova, N. A. Change in Energetics of Muscular Contraction as a Result of Hyperoxia, 4(77).

Rippstein, W. J. and Coleman, M. E. Toxicological Evaluation of Columbia Spacecraft, 4(87).

Rogacheva, I. V., Stupakov, G. P., Volozhin, A. I., Pavlova, M. N. and Polyakov, A. N. Rat Bone Tissue After Flight Aboard Cosmos-1129 Biosatellite, 5(39).

Savina, Ye. A., Pankova, A. S., Kabitskaya, O. Ye., Belkaniya, G. S. and Tavadyan, D. S. Primate Adrenal Reactions to Antiorthostatic Hypokinesia, 5(30).

Saulgozis, Yu. Zh., Novikov, V. Ye., Dobelis, M. A., Il'in, Ye. A. and Lebedev, V. I. Ultrasound Distribution and Bone Calcium Content in Experimental Animals Submitted to Hypokinesia and Weightlessness, 3(48).

Sivuk, A. K., Mosyakina, L. I., Malevskaya-Malevich, N. A., Ul'yanova, I. A., Sedova, Ye. A. and Kravchuk, A. N. Effect of High Ammonia Content in Closed Environment on Some Parameters of Human Nitrogen and Carbohydrate Metabolism Against Background of a Controlled Diet, 6(69).

Smirnov, K. V., Petrusenko, A. N. and Menshchikov, A. P. Human Stomach Motor and Evacuatory Functions During Antiorthostatic Hypokinesia, 3(34).

Smirnova, T. M. Potential Use of Dialogue With Computers in Biomedical Research, 4(16).

Sobolevskiy, V. I. and Pravosudov, V. P. Circulatory Changes in Orthostatic Position in the Presence of Hyperthermia, 3(23).

Sobolevskiy, V. I. and Pravosudov, V. P. Preventive Effect of Acute Heat Factors During Hypokinesia, 6(58).

Sokolov, V. I. Reaction of Cerebral Ventricles to Antiorthostatic Position and Occlusion of Jugular Veins, 4(66).

Stupakov, G. P., Kazeykin, V. S., Kozlovskiy, A. P. and Korolev, V. V. Evaluation of Changes in Human Axial Skeletal Bone Structures During Long-Term Spaceflights, 2(33).

Taylor, G. R. and Dardano, J. R. Human Cellular Immune Responsiveness Following Spaceflight, 1(74).

Terelyak, Ya. Some Psychological Consequences of Prolonged Social Isolation 2(54).

Tigranyan, R. A., Vakulina, O. P. and Panchenko, L. F. Effect of Short-Term Hypokinesia on Rat Opioid System Reaction, 4(63).

Tigranyan, R. A., Voronin, L. I. and Kalita, N. F. Biochemical Status of Adrenocortical Dysfunction Following Spaceflight, 6(18).

Tikunov, B. A., Kayfadzhyan, M. A. and Oganesyan, S. S. Effect of Periodic Accelerations on Physicochemical Properties and Ca^{2+} Reactivity of Actomyosin in White Rat Myocardium and Skeletal Muscles, 5(44).

Tikhomirova, M. V., Yashkin, P. N., Fedorenko, B. S. and Chertkov, K. S. Radioprotective Efficacy of ATP and Adenosine With Exposure to High-Energy Protons, 5(75).

Tyvin, L. I. Effect of Stationary Magnetic Field on Bioelectric Activity of Rabbit Brain Epileptogenic Foci, 3(71).

Shul'zhenko, Ye. B., Kozlova, V. G., Aleksandrova, Ye. A. and Kudrin, K. A. Adaptive Effects of Repeated Immersion on Man, 2(57).

Shchukin, A. I. Effect of Working in Two Shifts on Circadian Rhythm of Heart Rate, 2(63).

Shchukin, A. I. Circadian Dynamics of Potassium Excretion in Urine as Related to Working on One and Two Shifts, 5(58).

Yarullin, Kh. Kh., Vasil'yeva, T. D., Turchaninova, V. F., Sokolova, I. V. and Vikharev, N. D. Compensatory and Adaptive Regional Hemodynamic Reactions to Weightlessness During Long-Term Spaceflights, 4(22).

Methods

Zhuravlev, V. V. Spirolit-2 Instrument Used to Test Pulmonary Ventilation, 6(76).

Katkov, V. Ye. and Rumyantsev, V. V. Nomogram for Demonstrating Change in Central Venous and Pulmonary Artery Pressure During Decompression of Different Parts of the Body, 3(89).

Pozharskiy, G. O. Method of Determining Intensity of Elimination of Microorganisms From Human Upper Respiratory Tract, 2(78).

Rustam'yan, O. N. and Vasil'yev, V. K. Model of Information-Reference Dialogue System for Working With Document Abstracts, 6(73).

Brief Reports

Alekseyev, Ye. I., Savina, Ye. A. and Belkaniya, G. S. Morphological Study of Primate Hypothalamus and Hypophysis After Experiment With Antiorthostatic Hypokinesia, 5(78).

Volkind, N. Ya. Effect of Exam Stress on Cardiac Function of Students Differing in Level of Physical Activity, 2(86).

Gora, Ye. P. Individual Distinctions of Human Sleeping Respiration at Altitude of 4200 Meters, 3(93).

Gorchinskaya, E. Effect of Stationary Magnetic Field on Bleeding Time, 6(87).

Kozlova, V. G. and Il'ina, Ye. A. Muscle Tone Changes in Individuals of Different Age Groups Submitted to Simulated Weightlessness, 1(90).

Kokoreva, L. V. Effect of Long-Term Repeated Exposure to High-Intensity Stationary Magnetic Field on Adrenomedullary Activity, 6(86).

Korol'kov, V. I., Viktorov, A. N., Petrova, L. N., Knyazev, V. M. and Stelingovskiy, K. V. Results of Sanitary-Microbiological Studies Aboard Cosmos-936 and Cosmos-1129 Biosatellites, 6(79).

Koryukin, V. Ye. and Usachev, V. I. Influence of Limboreticular Complex on Some Vestibular Reactions of Rabbits, 5(88).

Kuz'mina, Z. F. Mouse Adrenal Corticosterone Content During Prolonged Exposure to High-Intensity Stationary Magnetic Field, 2(87).

Lunina, N. V. and Poltavskiy, A. F. Dependence of Blood Coagulating and Fibrinolytic Systems on Functional State of Lysosomal System of Neutrophil Leukocytes During Exposure of the Body to Low Barometric Pressure, 3(90).

Oygenblik, E. A. Effect of Centrifuging on Survival of Early Larvae of Common Frogs, 2(82).

Pankova, A. S. and Pal'tsev, M. A. Changes in Nephron and Juxtaglomerular System of Primate Kidneys Under the Effect of Antiorthostatic Hypokinesia, 5(83).

Polikarpov, N. A. and Shilov, V. M. Dynamics of Quantitative and Qualitative Changes in Conditionally Pathogenic Microflora of the Human Intestine During Long-Term Hypokinesia, 6(81).

Popova, I. A., Vetrova, Ye. G. and Drozdova, T. Ye. Blood Serum Enzyme Activity Following Long-Term Spaceflights, 5(81).

Popova, I. A., Drozdova, T. N. and Vetrova, Ye. G. Parameters of Carbohydrate Metabolism and Blood Serum Enzyme Activity After Short-Term Spaceflights, 6(78).

Potapov, P. P. and Tikhomirova, N. A. Rat Blood Serum and Liver Carbohydrates and Lipids in Recovery Period After 15-Day Hypokinesia, 5(87).

Prisenko, V. G. Canine Liver Nucleic Acid Content During Long-Term Experimental Hypokinesia, 2(85).

Rumyantsev, V. V. and Katkov, V. Ye. Simulation of Physiological Effects of Negative Pressure on Man, 3(92).

Tigranyan, R. A. and Vakulina, O. P. Rat Tissue Opioid Peptide Content During Long-Term Hypokinesia, 6(83).

Tigranyan, R. A. and Vetrova, Ye. G. Oxidative Enzyme Activity in Rat Blood Plasma and Subcellular Fraction of Liver Following Flight Aboard Cosmos-936 Biosatellite, 2(81).

Shikina, M. I., Aladinskaya, T. I., Chizhov, S. V., Sinyak, Yu. Ye. and Orlovskiy, S. P. Artificial Mineralization of Glacier Melt to be Used for Drinking During Mountain Expeditions at High Altitudes, 3(95).

Current Events and Information

Gyurdzhian, A. A., Ledovskoy, S. M. and Savchenko, V. I. Thirteenth Gagarin Conference, 1(92).

Kozlovskaya, I. B., Genin, A. M., Grigor'yev, A. I. and Il'in, Ye. A. Fifth International Symposium on Gravitational Physiology, 5(91).

Book Reviews

Antipov, V. V. and Davydov, B. I. "Space Radiobiology" by Yu. G. Grigor'yev, 2(89).

Vasil'yev, P. V. "Physiological Studies in Weightlessness," edited by P. V. Simonov and I. I. Kas'yan, Moscow, Meditsina, 1983, 304 pages, 5(90).

Gyurdzhian, A. A. and Tokarev, V. F. "Clinical Aviation Medicine," by R. B. Rayman, New York, Vantage Press, 1982, 245 pages, 6(89).

Kovalenko, Ye. A. and Kondrat'yev, Yu. I. "Metabolism Under Hypodynamic Conditions," by I. V. Fedorov, 2(92).

Panova, E. M. and Tokarev, V. F. "Medication and Flying. A Pilot's Guide," by S. Mohler, Boston Publishing Company, Boston, MA, United States, 1982, 214 pages, 6(91).

Anniversaries

Aleksandr Aleksandrovich Sergeyev (on his 90th Birthday), 6(93).

Obituaries, 2(94), 5(95).

Synopses of Articles Filed With the All-Union Scientific Research Institute of Medical and Medicotechnical Information and All-Union Institute of Scientific and Technical Information, Nos 2, 5, 6.

AUTHOR INDEX: KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA VOLUME 18, NUMBERS 1-6, 1984

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 19, No 1, Jan-Feb 85 (signed to press 7 Dec 84) pp 92-93

[Text] Abdrakhmanov, V. R., 5(23)
Abrosimov, S. V., 3(19)
Agadzhanyan, N. A., 3(65)
Aladinskaya, T. I., 3(95)
Aleksandrova, Ye. A., 2(57)
Alekseyev, D. A., 4(29, 81)
Alekseyev, Ye. I., 5(78)
Aleshin, S. V., 5(14)
Amirkhanyan, Ye. A., 2(73)
Anashkin, O. D., 3(19)
Andretsov, V. A., 6(29)
Antipov, V. V., 2(89), 4(43)
Artamonova, N. P., 4(29)

Batechuk-Tusko, T. V., 2(40)
Bayev, I. A., 4(41)
Bayrakova, A. K., 4(41)
Bazunova, Ye. G., 6(48)
Bebyakova, N. A., 4(77)
Bednenko, V. S., 2(50)
Belakovskiy, M. S., 3(4), 4(19, 49), 5(10)
Belkaniya, G. S., 2(73), 3(14), 5(30, 78), 6(44, 62)
Belozerov, G. Ye., 3(9)
Belozerova, I. N., 6(26)
Benova, D. K., 4(41)
Berkovskaya, M. I., 6(40)
Bogdanov, N. G., 3(4), 4(19), 5(10)
Bogomolov, V. V., 5(34)
Bogushevich, M. S., 5(34)
Brilene, T. A., 2(38)
Brilis, V. I., 2(38)
Britvan, I. I., 4(12)
Bychkov, V. P., 3(75)

Chebotarev, N. D., 4(69)
Chekanova, S. L., 6(33)
Chel'naya, N. A., 4(12)
Chernyy, A. V., 4(55)
Chertkov, K. S., 5(75)
Chestukhin, V. V., 1(80), 6(40)
Chichagov, P. K., 3(52)
Chizhov, S. V., 3(95)
Coleman, M. E., 4(87)

Dardano, J. R., 1(74)
Dartsmeliya, V. A., 3(14)
Davydov, B. I., 2(7, 89), 3(68)
Degterenkova, N. V., 5(54)
Denisov, A. F., 5(62)
Dietlein, L. F., 1(8)
Dmitriyeva, N. P., 2(73)
Dobelis, M. A., 3(48)
Doronina, T. D., 3(52)
Doroshev, V. G., 6(33)
Draguzya, M. D., 3(57)
Drobyshev, V. I., 4(43)
Drobyshevskaya, T. A., 2(43)
Drozdova, T. Ye., 5(81), 6(78)
Durnova, G. N., 6(44)
D'yakonov, A. S., 5(71)

Fedorenko, B. S., 5(75)
Filatova, L. M., 4(29)
Finogenova, R. I., 3(9)
Fotina, L. A., 4(29)
Frenkel', I. D., 3(75)

Gal'chin, V. V., 5(34)
Galichiy, V. A., 3(9)
Galkin, A. A., 2(7), 3(68)

Gazenko, O. G., 1(3, 14), 2(22)
Genin, A. M., 1(14), 2(22), 3(9), 5(91)
Gevlich, G. I., 5(26), 6(22)
Gippenreyter, Ye. B., 3(4)
Glod, G. D., 4(37)
Golikov, A. P., 5(23)
Goncharov, I. B., 5(23)
Gora, Ye. P., 3(93)
Gorchinskaya, E., 6(87)
Gornago, V. A., 4(29), 5(54)
Grechikhin, G. N., 2(50)
Grigor'yev, A. I., 5(91)
Grigor'yeva, L. S., 6(22)
Gulyayev, V. N., 5(10)
Gurovskiy, N. N., 2(22)
Gvozdev, S. V., 1(80), 6(40)
Gyurdzhian, A. A., 1(92), 6(89)

Il'in, Ye. A., 1(57), 3(48), 5(91)
Il'ina, Ye. A., 1(90)
Il'ina-Kakuyeva, Ye. I., 2(71)
Ivanov, G. G., 5(34)
Ivanov, L. A., 4(69)
Ivanov, V. A., 5(10)

Kabitskaya, O. Ye., 4(49), 5(30)
Kalandarov, S., 3(75)
Kalinichenko, V. V., 5(7)
Kalita, N. F., 6(18)
Kamenskiy, Yu. N., 2(47), 6(37)
Kan, Ye. L., 5(62)
Kaplanskiy, A. S., 4(49), 6(44)
Karpov, V. N., 2(7)
Kas'yan, I. I., 6(4)
Katkov, V. Ye., 1(80), 3(89, 92), 6(40)
Katuntsev, V. P., 3(9, 52)
Katyukhin, L. N., 3(43)
Kayfadzhyan, M. A., 5(44)
Kazakova, R. T., 3(52)
Kazeykin, V. S., 2(33)
Kediya, T. G., 6(40)

Khayutin, V. M., 4(4)
Kheymets, G. I., 3(9)
Khomenko, M. N., 4(37)

Kirillova, Z. A., 6(33)
Klimovskaya, L. D., 5(71)
Knyazev, V. M., 6(79)
Kokoreva, L. V., 6(86)
Kokova, N. I., 4(33)
Kolpakova, N. F., 3(38)
Kondrat'yev, Yu. I., 2(92)
Kopanev, V. I., 3(57)
Korolev, V. V., 2(33)
Korol'kov, V. I., 4(12), 6(79)
Koryukin, V. Ye., 5(88)
Kovachevich, I. V., 5(23)
Kovalenko, Ye. A., 2(92)
Kovalev, Ye. Ye., 1(36)
Kozinets, G. I., 4(12)
Kozlov, A. N., 2(50)
Kozlova, V. G., 1(90), 2(57)
Kozlovskaya, I. B., 5(91), 6(22)
Kozlovskiy, A. P., 2(33)
Kravchuk, A. N., 6(69)
Krotov, V. P., 6(48)
Krupina, T. N., 4(29, 81)
Krylov, Yu. V., 5(4)
Kudrin, K. A., 2(57)
Kudryashova, Zh. M., 5(34)
Kukushkin, Yu. A., 6(67)
Kulayev, B. S., 6(48)
Kuleshov, V. I., 4(73)
Kupriyanov, V. A., 5(62)
Kustov, V. V., 6(67)
Kuz'min, M. P., 4(29, 81)
Kuz'mina, Z. F., 2(87)
Kuznets, Ye. I., 4(81)
Kuznetsova, T. I., 3(75)

Landukhova, N. F., 2(67)
Latskevich, A. A., 2(26), 3(25), 6(10)
Leach, C. S., 1(29, 67)
Lebedev, V. I., 3(48)
Ledovskoy, S. M., 1(92)
Legen'kov, V. I., 2(38)
Lenskiy, V. V., 5(34)
Lentsner, A. A., 2(38)
Lentsner, Kh. P., 2(38)
Lhagwa, L., 2(60), 6(15)
Litau, V. G., 6(67)
Liz'ko, N. N., 2(38)
Lobachik, V. I., 3(19)
Lobova, T. M., 4(55)
Loginova, Ye. V., 5(47)
Lozinskiy, P. A., 3(80)
Luk'yanyuk, V. Yu., 5(18)
Lunina, N. V., 3(90)
Lustin, S. I., 3(57)

Makarov, G. F., 6(4)
Makarov, V. V., 4(43)
Maksimov, D. G., 3(9)
Malevskaya-Malevich, N. A., 6(69)
Malinovskaya, O. O., 5(62)
Malkin, V. B., 2(67), 5(47)
Mansfel'd, A. D., 3(52)
Maslova, M. N., 3(43)
Matrosova, M. A., 6(33)
Menshchikov, A. P., 3(34)
Mikhaylov, V. M., 6(29)
Miroshnikova, N. B., 6(26)
Modin, A. Yu., 3(19), 5(54)
Mogutov, S. S., 3(61)
Moseley, E., 1(29)
Mosyakina, L. I., 6(69)
Mukhamediva, L. N., 2(40)

Namlinskiy, Yu. V., 4(73)
Nefedov, Yu. G., 2(22, 40)
Nicogossian, A., 1(8, 29, 45)
Nikolayenko, E. M., 1(80), 6(40)
Nikolayev, V. P., 3(52)
Nikolov, Kh. G., 4(41)
Nosova, I. M., 2(43)
Novikov, V. Ye., 3(48)

Obukhova, M. V., 3(9)
Oganesyan, S. S., 5(44)
Orlovskiy, S. P., 3(95)
Osadchiyeva, N. A., 2(43)
Oygenblik, E. A., 2(82)

Pal'tsev, M. A., 5(83)
Panasyuk, Ye. N., 4(58)
Panchenko, L. F., 4(63)
Pankova, A. S., 5(30, 83)
Panova, E. M., 6(91)
Parfenov, G. P., 5(68)
Parshin, L. B., 3(19)
Pas, I. A., 3(65)
Pavlova, M. N., 5(39)
Pchelenko, L. D., 4(77)
Petrova, L. N., 6(79)
Petrusenko, A. N., 3(34)
Plakhuta-Plakutina, G. I., 2(73)
Polikarpov, N. A., 6(81)
Poltavskiy, A. F., 3(90)
Polyakov, A. N., 5(39)
Pometov, D. Yu., 6(29)
Pool, S. L., 1(29, 45)
Popov, I. G., 2(26), 3(25), 3(80), 6(10)
Popov, V. I., 6(44)
Popova, I. A., 5(81), 6(78)
Potapov, P. P., 4(55), 5(87)
Pozharskiy, G. O., 2(78), 3(77)
Pravosudov, V. P., 3(23), 6(58)
Prisenko, V. G., 2(85)

Radchenko, N. D., 4(19)
Rambaut, P., 1(8, 29)
Razinkin, S. M., 6(67)
Reyman, A. M., 3(52)
Rippstein, W. J., 4(87)
Rogacheva, I. V., 5(39)
Rogoza, A. N., 4(4)
Rolik, I. S., 4(37)
Romanova, I. A., 3(80)
Rumyantsev, V. V., 1(80), 3(89, 92)
Rustam'yan, O. N., 6(73)

Safronov, A. M., 5(14)
Saulgozis, Yu. Zh., 3(48)
Savchenko, V. I., 1(92)
Savik, Z. F., 4(49), 6(44)
Savina, V. P., 2(40)
Savina, Ye. A., 2(73), 5(30, 78)
Sedova, Ye. A., 6(69)
Senkevich, Yu. A., 5(10)
Sergeyev, I. N., 4(49)
Sergeyeva, Ye. S., 3(61)
Severin, A. Ye., 3(65)

Shashkov, V. S., 3(19), 5(54)
Shchukin, A. I., 2(63), 5(58)
Shenderov, S. M., 4(4)
Shikina, M. I., 3(95)
Shilov, V. M., 2(38), 6(81)
Shul'zhenko, Ye. B., 2(57)
Shvets, V. N., 4(12, 49)

Sinyak, Yu. Ye., 3(95)
Sivuk, A. K., 6(69)
Skakun, L. N., 4(58)
Smirnov, K. V., 3(34)
Smirnov, O. A., 4(29)
Smirnova, T. M., 4(16)
Sobolevskiy, V. I., 3(23), 6(58)
Sokolov, V. I., 4(66), 5(54)
Sokolova, I. V., 4(22)
Spirichev, V. B., 4(49)
Stazhadze, L. L., 5(23, 34)

Stelingovskiy, K. V., 6(79)
Stupakov, G. P., 2(33), 5(39)
Syrykh, G. D., 2(38)

Tabak, V. Ya., 5(34)
Tavadyan, D. S., 2(73), 5(30), 6(44)
Taylor, G. R., 1(74)
Terelyak, Ya., 2(54)
Tigranyan, R. A., 2(81), 4(63), 6(18, 83)
Tikhomirova, M. V., 5(75)
Tikhomirova, N. A., 5(87)
Tikhonchuk, V. S., 3(68)
Tikunov, B. A., 5(44)
Tokarev, V. F., 6(89, 91)
Tsyganova, N. I., 4(29)
Turchaninova, V. F., 4(22)
Tyvin, L. I., 3(71)

Uglova, N. N., 4(37)
Ul'yanova, I. A., 6(69)
Urmancheyeva, T. G., 3(38)
Usachev, V. I., 5(88)
Ushakov, A. S., 3(4), 6(26)
Ushakov, I. B., 3(68)

Vabishchevich, A. V., 5(23)
Vacek, A., 4(12)
Vakulina, O. P., 4(63), 6(83)
Varnashenko, A. P., 6(33)
Vartbaronov, R. A., 4(37)
Vasil'yev, P. V., 5(90)
Vasil'yev, V. K., 6(73)
Vasil'yeva, T. D., 4(22), 5(26)
Vetrova, Ye. G., 2(81), 5(81), 6(78)
Vikharev, N. D., 4(22, 29)
Vikhrov, N. I., 6(33)
Viktorov, A. N., 2(40), 6(79)
Vlasova, T. F., 6(26)
Volkind, N. Ya., 2(86)
Volkova, M. I., 6(40)
Volozhin, A. I., 5(39)
Vorob'yev, V. Ye., 5(23)
Vorob'yev, Ye. I., 1(14), 2(22)
Vorona, A. A., 5(14)
Voronin, L. I., 6(18)
Voronina, S. G., 5(23)
Vorotnikova, Ye. V., 5(50), 6(54)
Voskoboynikov, V. A., 5(10)
Voskresenskiy, A. D., 6(33)
Vostrikov, V. A., 5(34)
Vysotskaya, V. R., 5(26)
Vytchikova, M. A., 2(40)

Yarullin, Kh. Kh., 4(22, 29, 81)
Yashkin, P. N., 5(75)

Yegorov, A. D., 1(14), 2(22)
Yelfimov, A. I., 3(65)
Yevgraf'yev, V. P., 3(61)

Yurova, K. S., 3(9, 52)

Zakharenko, T. S., 5(10)
Zakharov, A. G., 4(4)
Zaloguyev, S. N., 2(40)

Zhernavkov, A. F., 5(7)
Zhidkov, V. V., 3(19)
Zhuravlev, V. V., 6(76)
Zhvalikovskaya, V. P., 5(68)

Zingerman, L. S., 3(9)
Zubarev, A. F., 4(81)

10,657
CSO: 1849/3

- END -